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(54) Title: NOVEL G PROTEIN-COUPLED RECEPTORS

(57) Abstract: The present invention provides a gene encoding a G protein-coupled receptor termed nGPCR-x; constructs and recombinant host cells incorporating the genes; the nGPCR-x polypeptides encoded by the gene; antibodies to the nGPCR-x polypeptides; and methods of making and using all of the foregoing.

NOVEL G PROTEIN-COUPLED RECEPTORS

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] The present application claims priority of Application Serial No. 60/189,783, filed 2000 March 16; Application Serial No. 60/189,918 filed 2000 March 16; Application Serial No. 60/189,960 filed 2000 March 16; Application Serial No. 60/189,917 filed 2000 March 16; Application Serial No. 60/189,907 filed 2000 March 16; Application Serial No. 60/192,945 filed 2000 March 29; Application Serial No. 60/192,916 filed 2000 March 29; Application Serial No. 60/192,923 filed 2000 March 29; Application Serial No. 60/192,933 filed 2000 March 29; Application Serial No. 60/192,830 filed 2000 March 29; Application Serial No. 60/192,234 filed 2000 March 29; Application Serial No. 60/192,155 filed 2000 March 29; Application Serial No. 60/192,935 filed 2000 March 29; each of which is hereby incorporated by reference in its entirety.

FIELD OF THE INVENTION

[0002] The present invention relates generally to the fields of genetics and cellular and molecular biology. More particularly, the invention relates to novel G protein coupled receptors, to polynucleotides that encode such novel receptors, to reagents such as antibodies, probes, primers and kits comprising such antibodies, probes, primers related to thesame, and to methods which use the novel G protein coupled receptors, polynucleotides or reagents.

BACKGROUND OF THE INVENTION

[0003] The G protein-coupled receptors (GPCRs) form a vast superfamily of cell surface receptors which are characterized by an amino-terminal extracellular domain, a carboxyl-terminal intracellular domain, and a serpentine structure that passes through the cell membrane seven times. Hence, such receptors are sometimes also referred to as seven transmembrane (7TM) receptors. These seven transmembrane domains define three extracellular loops and three intracellular loops, in addition to the amino- and carboxy- terminal domains. The extracellular portions of the receptor have a role in recognizing and binding one or more extracellular binding partners (*e.g.*, ligands), whereas the intracellular portions have a role in recognizing and communicating with downstream molecules in the signal transduction cascade.

[0004] The G protein-coupled receptors bind a variety of ligands including calcium ions, hormones, chemokines, neuropeptides, neurotransmitters, nucleotides, lipids, odorants, and even photons, and are important in the normal (and sometimes the aberrant) function of many cell types. [See generally Strosberg, *Eur. J. Biochem.* 196:1-10 (1991) and Bohm*et al., Biochem J.* 322:1-18 (1997).] When a specific ligand binds to its corresponding receptor, the ligand typically stimulates the receptor to activate a specific heterotrimeric guanine-nucleotide-binding regulatory protein (G-protein) that is coupled to the intracellular portion of the receptor. The G protein in turn transmits a signal to an effector molecule within the cell, by either stimulating or inhibiting the activity of that effector molecule. These effector molecules include adenylate cyclase, phospholipases and ion channels. Adenylate cyclase and phospholipases are enzymes that are involved in the production of the second messenger molecules cAMP, inositol triphosphate and diacyglycerol. It is through this sequence of events that an extracellular ligand stimuli exerts intracellular changes through a G protein-coupled receptor. Each such receptor has its own characteristic primary structure, expression pattern, ligand-binding profile, and intracellular effector system.

[0005] Because of the vital role of G protein-coupled receptors in the communication between cells and their environment, such receptors are attractive targets for therapeutic intervention, for example by activating or antagonizing such receptors. For receptors having a known ligand, the identification of agonists or antagonists may be sought specifically to enhance or inhibit the action of the ligand. Some G protein-coupled receptors have roles in disease pathogenesis (*e.g*, certain chemokine receptors that act as HIV co-receptors may have a role in AIDS pathogenesis), and are attractive targets for therapeutic intervention even in the absence of knowledge of the natural ligand of the receptor. Other receptors are attractive targets for therapeutic intervention by virtue of their expression pattern in tissues or cell types that are themselves attractive targets for therapeutic intervention. Examples of this latter category of receptors include receptors expressed in immune cells, which can be targeted to either inhibit autoimmune responses or to enhance immune responses to fight pathogens or cancer; and receptors expressed in the brain or other neural organs and tissues, which are likely targets in the treatment of mental disorder, depression, bipolar disease, or other neurological disorders. This latter category of receptor is also useful as a marker for identifying and/or purifying (*e.g.*, via fluorescence-activated cell sorting) cellular subtypes that express the receptor. Unfortunately, only a limited number of G protein receptors from the central nervous system (CNS) are known. Thus, a need exists for G protein-coupled receptors that have been identified and show promise as targets for therapeutic intervention in a variety of animals, including humans.

SUMMARY OF THE INVENTION

[0006] The present invention relates to an isolated nucleic acid molecule that comprises a nucleotide sequence that encodes a polypeptide comprising an amino acid sequence homologous to sequences selected from the group consisting of SEQ ID NO:129 to SEQ IDNO:257, or a fragment thereof. The nucleic acid molecule encodes at least a portion of nGPCR-x. In some embodiments, the nucleic acid molecule comprises a sequence that encodes a polypeptide comprising a sequence selected from the group consisting of SEQ ID NO:129 to SEQ ID NO:257, or a fragment thereof. In some embodiments, the nucleic acid molecule comprises a sequence homologous to a sequence selected from the group consisting of SEQ ID NO:1 to SEQ ID NO:128, or a fragment thereof. In some embodiments, the nucleic acid molecule comprises a sequence selected from the group consisting of SEQ ID NO:1 to SEQ ID NO:128, and fragments thereof.

[0007] According to some embodiments, the present invention provides vectors which comprise the nucleic acid molecule of the invention. In some embodiments, the vector is an expression vector.

[0008] According to some embodiments, the present invention provides host cells which comprise the vectors of the invention. In some embodiments, the host cells comprise expression vectors.

[0009] The present invention provides an isolated nucleic acid molecule comprising a nucleotide sequence complementary to at least a portion of a sequence selected from the group consisting of SEQ ID NO:1 to SEQ ID NO:128, said portion comprising at least 10 nudeotides.

[00010] The present invention provides a method of producing a polypeptide comprising a sequence selected from the group consisting of SEQ ID NO:129 to SEQ ID NO:257, or a homolog or fragment thereof. The method comprising the steps of introducing a recombinant expression vector that includes a nucleotide sequence that encodes the polypeptide into a compatible host cell, growing the host cell under conditions for expression of the polypeptide and recovering the polypeptide.

[00011] The present invention provides an isolated antibody which binds to an epitope on a polypeptide comprising a sequence selected from the group consisting of SEQ ID NO:129 to SEQ ID NO:257, or a homolog or fragment thereof.

[00012] The present invention provides an method of inducing an immune response in a mammal against a polypeptide comprising a sequence selected from the group consisting of SEQ ID NO:129 to SEQ ID NO:257, or a homolog or fragment thereof. The method comprises

administering to a mammal an amount of the polypeptide sufficient to induce said immune response.

[00013] The present invention provides a method for identifying a compound which binds nGPCR-x. The method comprises the steps of contacting nGPCR-x with a compound and determining whether the compound binds nGPCR-x.

[00014] The present invention provides a method for identifying a compound which binds a nucleic acid molecule encoding nGPCR-x. The method comprises the steps of contacting said nucleic acid molecule encoding nGPCR-x with a compound and determining whether said compound binds said nucleic acid molecule.

[00015] The present invention provides a method for identifying a compound which modulates the activity of nGPCR-x. The method comprises the steps of contacting nGPCR-x with a compound and determining whether nGPCR-x activity has been modulated.

[00016] The present invention provides a method of identifying an animal homolog of nGPCR-x. The method comprises the steps screening a nucleic acid database of the animal with a sequence selected from the group consisting of SEQ ID NO:1 to SEQ ID NO:128, or a portion thereof and determining whether a portion of said library or database is homologous to said sequence selected from the group consisting of SEQ ID NO:1 to SEQ ID NO:128, or portion thereof.

[00017] The present invention provides a method of identifying an animal homolog of nGPCR-x. The methods comprises the steps screening a nucleic acid library of the animal with a nucleic acid molecule having a sequence selected from the group consisting of SEQ ID NO:1 to SEQ ID NO:128, or a portion thereof; and determining whether a portion of said library or database is homologous to said sequence selected from the group consisting of SEQ ID NO:1 to SEQ ID NO:128, or a portion thereof.

[00018] Another aspect of the present invention relates to methods of screening a human subject to diagnose a disorder affecting the brain or genetic predisposition therefor. The methods comprise the steps of assaying nucleic acid of a human subject to determine a presence or an absence of a mutation altering an amino acid sequence, expression, or biological activity of at least one nGPCR-x that is expressed in the brain. The nGPCR-x comprise an amino acid sequence selected from the group consisting of SEQ ID NO:129 to SEQ ID NO:257, and allelic variants thereof. A diagnosis of the disorder or predisposition is made from the presence or absence of the mutation. The presence of a mutation altering the amino acid sequence, expression, or biological activity of the nGPCR-x in the nucleic acid correlates with an increased risk of developing the disorder.

[00019] The present invention further relates to methods of screening for a nGPCR-x hereditary mental disorder genotype in a human patient. The methods comprise the steps of providing a

biological sample comprising nucleic acid from the patient, in which the nucleic acid includes sequences corresponding to alleles of nGPCR-x. The presence of one or more mutations in the nGPCR-x allele is indicative of a hereditary mental disorder genotype.

[00020] The present invention provides kits for screening a human subject to diagnose mental disorder or a genetic predisposition therefor. The kits include an oligonucleotide useful as a probe for identifying polymorphisms in a human nGPCR-x gene. The oligonucleotide comprises 6-50 nucleotides in a sequence that is identical or complementary to a sequence of a wild type human nGPCR-x gene sequence or nGPCR-x coding sequence, except for one sequence difference selected from the group consisting of a nucleotide addition, a nucleotide deletion, or nucleotide substitution. The kit also includes a media packaged with the oligonucleotide. The media contains information for identifying polymorphisms that correlate with mental disorder or a genetic predisposition therefor, the polymorphisms being identifiable using the oligonucleotide as a probe.

[00021] The present invention further relates to methods of identifying nGPCR-x allelic variants that correlates with mental disorders. The methods comprise the steps of providing biological samples that comprise nucleic acid from a human patient diagnosed with a mental disorder, or from the patient's genetic progenitors or progeny, and detecting in the nucleic acid the presence of one or more mutations in an nGPCR-x that is expressed in the brain. The nGPCR-x comprises an amino acid sequence selected from the group consisting of SEQ ID NO:129 to SEQ ID NO:257, and allelic variants thereof. The nucleic acid includes sequences corresponding to the gene or genes encoding nGPCR-x. The one or more mutations detected indicate an allelic variant that correlates with a mental disorder.

[00022] The present invention further relates to purified polynucleotides comprising nucleotide sequences encoding alleles of nGPCR-x from a human with mental disorder. The polynucleotide hybridizes to the complement of a sequence selected from the group consisting of SEQ ID NO:1 to SEQ ID NO:128 under the following hybridization conditions: (a) hybridization for 16 hours at 42°C in a hybridization solution comprising 50% formamide, 1% SDS, 1 M NaCl, 10% dextran sulfate and (b) washing 2 times for 30 minutes at 60°C in a wash solution comprising 0.1x SSC and 1% SDS. The polynucleotide that encodes nGPCR-x amino acid sequence of the human differs from a sequence selected from the group consisting of SEQ ID NO:129 to SEQ ID NO:257 by at least one residue.

[00023] The present invention also provides methods for identifying a modulator of biological activity of nGPCR-x comprising the steps of contacting a cell that expresses nGPCR-x in the presence and in the absence of a putative modulator compound and measuring nGPCR-x biological activity in the cell. The decreased or increased nGPCR-x biological activity in the

presence versus absence of the putative modulator is indicative of a modulator of biological activity.

[00024] The present invention further provides methods to identify compounds useful for the treatment of mental disorders. The methods comprise the steps of contacting a composition comprising nGPCR-x with a compound suspected of binding nGPCR-x. The binding between nGPCR-x and the compound suspected of binding nGPCR-x is detected. Compounds identified as binding nGPCR-x are candidate compounds useful for the treatment of mental disorder. Compounds identified as binding nGPCR-x may be further tested in other assays including, but not limited to, *in vivo* models, in order to confirm or quantitate their activity.

[00025] The present invention further provides methods for identifying a compound useful as a modulator of binding between nGPCR-x and a binding partner of nGPCR-x. The methods comprise the steps of contacting the binding partner and a composition comprising nGPCR-x in the presence and in the absence of a putative modulator compound and detecting binding between the binding partner and nGPCR-x. Decreased or increased binding between the binding partner and nGPCR-x in the presence of the putative modulator, as compared to binding in the absence of the putative modulator is indicative a modulator compound useful for the treatment of a related disease or disorder. Compounds identified as modulating binding between nGPCR-x and a nGPCR-x binding partner may be further tested in other assays including, but not limited to, *in vivo* models, in order to confirm or quantitate their activity as modulators.

[00026] Another aspect of the present invention relates to methods of purifying a G protein from a sample containing a G protein. The methods comprise the steps of contacting the sample with an nGPCR-x for a time sufficient to allow the G protein to form a complex with the nGPCR-x; isolating the complex from remaining components of the sample; maintaining the complex under conditions which result in dissociation of the G protein from the nGPCR-x; and isolating said G protein from the nGPCR-x.

DETAILED DESCRIPTION OF PREFERRED EMBODIMENTS

Definitions

[00027] Various definitions are made throughout this document. Most words have the meaning that would be attributed to those words by one skilled in the art. Words specifically defined either below or elsewhere in this document have the meaning provided in the context of the present invention as a whole and as are typically understood by those skilled in the art.

[00028] "Synthesized" as used herein and understood in the art, refers to polynucleotides produced by purely chemical, as opposed to enzymatic, methods. "Wholly" synthesized DNA

sequences are therefore produced entirely by chemical means, and "partially" synthesized DNAs embrace those wherein only portions of the resulting DNA were produced by chemical means.

[00029] By the term "region" is meant a physically contiguous portion of the primary structure of a biomolecule. In the case of proteins, a region is defined by a contiguous portion of the amino acid sequence of that protein.

[00030] The term "domain" is herein defined as referring to a structural part of a biomolecule that contributes to a known or suspected function of the biomolecule. Domains may be co-extensive with regions or portions thereof; domains may also incorporate a portion of a biomolecule that is distinct from a particular region, in addition to all or part of that region . Examples of GPCR protein domains include, but are not limited to, the extracellular (*i.e.*, N-terminal), transmembrane and cytoplasmic (*i.e.*, C-terminal) domains, which are co-extensive with like-named regions of GPCRs; each of the seven transmembrane segments of a GPCR; and each of the loop segments (both extracellular and intracellular loops) connecting adjacent transmembrane segments.

[00031] As used herein, the term "activity" refers to a variety of measurable indicia suggesting or revealing binding, either direct or indirect; affecting a response, i.e. having a measurable affect in response to some exposure or stimulus, including, for example, the affinity of a compound for directly binding a polypeptide or polynucleotide of the invention, or, for example, measurement of amounts of upstream or downstream proteins or other similar functions after some stimulus or event.

[00032] Unless indicated otherwise, as used herein, the abbreviation in lower case (gpcr) refers to a gene, cDNA, RNA or nucleic acid sequence, while the upper case version (GPCR) refers to a protein, polypeptide, peptide, oligopeptide, or amino acid sequence. The term "nGPCR-x" refers to any of the nGPCRs taught herein, while specific reference to a nGPCR (for example nGPCR-2073) refers only to that specific nGPCR.

[00033] As used herein, the term "antibody" is meant to refer to complete, intact antibodies, and Fab, Fab', F(ab)2, and other fragments thereof. Complete, intact antibodies include monoclonal antibodies such as murine monoclonal antibodies, chimeric antibodies and humanized antibodies.

[00034] As used herein, the term "binding" means the physical or chemical interaction between two proteins or compounds or associated proteins or compounds or combinations thereof. Binding includes ionic, non-ionic, Hydrogen bonds, Van der Waals, hydrophobic interactions, etc. The physical interaction, the binding, can be either direct or indirect, indirect being through or due to the effects of another protein or compound. Direct binding refers to interactions that do not take place through or due to the effect of another protein or compound but instead are

without other substantial chemical intermediates. Binding may be detected in many different manners. As a non-limiting example, the physical binding interaction between a nGPCR-x of the invention and a compound can be detected using a labeled compound. Alternatively, functional evidence of binding can be detected using, for example, a cell transfected with and expressing a nGPCR-x of the invention. Binding of the transfected cell to a ligand of the nGPCR-x that was transfected into the cell provides functional evidence of binding. Other methods of detecting binding are well known to those of skill in the art.

[00035] As used herein, the term "compound" means any identifiable chemical or molecule, including, but not limited to, small molecule, peptide, protein, sugar, nucleotide, or nucleic acid, and such compound can be natural or synthetic.

[00036] As used herein, the term "complementary" refers to Watson-Crick basepairing between nucleotide units of a nucleic acid molecule.

[00037] As used herein, the term "contacting" means bringing together, either directly or indirectly, a compound into physical proximity to a polypeptide or polynucleotide of the invention. The polypeptide or polynucleotide can be in any number of buffers, salts, solutions *etc.* Contacting includes, for example, placing the compound into a beaker, microtiter plate, cell culture flask, or a microarray, such as a gene chip, or the like, which contains the nucleic acid molecule, or polypeptide encoding the nGPCR or fragment thereof.

[00038] As used herein, the phrase "homologous nucleotide sequence," or "homologous amino acid sequence," or variations thereof, refers to sequences characterized by a homology, at the nucleotide level or amino acid level, of at least the specified percentage. Homologous nucleotide sequences include those sequences coding for isoforms of proteins. Such isoforms can be expressed in different tissues of the same organism as a result of, for example, alternative splicing of RNA. Alternatively, isoforms can be encoded by different genes. Homologous nucleotide sequences include nucleotide sequences encoding for a protein of a species other than humans, including, but not limited to, mammals. Homologous nucleotide sequences also include, but are not limited to, naturally occurring allelic variations and mutations of the nucleotide sequences set forth herein. A homologous nucleotide sequence does not, however, include the nucleotide sequence encoding other known GPCRs. Homologous amino acid sequences include those amino acid sequences which contain conservative amino acid substitutions and which polypeptides have the same binding and/or activity. A homologous amino acid sequence does not, however, include the amino acid sequence encoding other known GPCRs. Percent homology can be determined by, for example, the Gap program (Wisconsin Sequence Analysis Package, Version 8 for Unix, Genetics Computer Group, University Research Park, Madison WI), using the default settings, which uses the algorithm of Smith and

Waterman (Adv. Appl. Math., 1981, 2, 482-489, which is incorporated herein by reference in its entirety).

[00039] As used herein, the term "isolated" nucleic acid molecule refers to a nucleic acid molecule (DNA or RNA) that has been removed from its native environment. Examples of isolated nucleic acid molecules include, but are not limited to, recombinant DNA molecules contained in a vector, recombinant DNA molecules maintained in a heterologous host cell, partially or substantially purified nucleic acid molecules, and synthetic DNA or RNA molecules.

[00040] As used herein, the terms "modulates" or "modifies" means an increase or decrease in the amount, quality, or effect of a particular activity or protein.

[00041] As used herein, the term "oligonucleotide" refers to a series of linked nucleotide residues which has a sufficient number of bases to be used in a polymerase chain reaction (PCR). This short sequence is based on (or designed from) a genomic or cDNA sequence and is used to amplify, confirm, or reveal the presence of an identical, similar or complementary DNA or RNA in a particular cell or tissue. Oligonucleotides comprise portions of a DNA sequence having at least about 10 nucleotides and as many as about 50 nucleotides, preferably about 15 to 30 nucleotides. They are chemically synthesized and may be used as probes.

[00042] As used herein, the term "probe" refers to nucleic acid sequences of variable length, preferably between at least about 10 and as many as about 6,000 nucleotides, depending on use. They are used in the detection of identical, similar, or complementary nucleic acid sequences. Longer length probes are usually obtained from a natural or recombinant source, are highly specific and much slower to hybridize than oligomers. They may be single- or double-stranded and carefully designed to have specificity in PCR, hybridization membrane-based, or ELISA-like technologies.

[00043] The term "preventing" refers to decreasing the probability that an organism contracts or develops an abnormal condition.

[00044] The term "treating" refers to having a therapeutic effect and at least partially alleviating or abrogating an abnormal condition in the organism.

[00045] The term "therapeutic effect" refers to the inhibition or activation factors causing or contributing to the abnormal condition. A therapeutic effect relieves to some extent one or more of the symptoms of the abnormal condition. In reference to the treatment of abnormal conditions, a therapeutic effect can refer to one or more of the following: (a) an increase in the proliferation, growth, and/or differentiation of cells; (b) inhibition (*i.e.*, slowing or stopping) of cell death; (c) inhibition of degeneration; (d) relieving to some extent one or more of the symptoms associated with the abnormal condition; and (e) enhancing the function of the

affected population of cells. Compounds demonstrating efficacy against abnormal conditions can be identified as described herein.

[00046] The term "abnormal condition" refers to a function in the cells or tissues of an organism that deviates from their normal functions in that organism. An abnormal condition can relate to cell proliferation, cell differentiation, cell signaling, or cell survival. An abnormal condition may also include obesity, diabetic complications such as retinal degeneration, and irregularities in glucose uptake and metabolism, and fatty acid uptake and metabolism.

[00047] Abnormal cell proliferative conditions include cancers such as fibrotic and mesangial disorders, abnormal angiogenesis and vasculogenesis, wound healing, psoriasis, diabetes mellitus, and inflammation.

[00048] Abnormal differentiation conditions include, but are not limited to, neurodegenerative disorders, slow wound healing rates, and slow tissue graftinghealing rates. Abnormal cell signaling conditions include, but are not limited to, psychiatric disorders involving excess neurotransmitter activity.

[00049] Abnormal cell survival conditions may also relate to conditions in which programmed cell death (apoptosis) pathways are activated or abrogated. A number of protein kinases are associated with the apoptosis pathways. Aberrations in the function of any one of the protein kinases could lead to cell immortality or premature cell death.

[00050] The term "administering" relates to a method of incorporating a compound into cells or tissues of an organism. The abnormal condition can be prevented or treated when the cells or tissues of the organism exist within the organism or outside of the organism. Cells existing outside the organism can be maintained or grown in cell culture dishes. For cells harbored within the organism, many techniques exist in the art to administer compounds, including (but not limited to) oral, parenteral, dermal, injection, and aerosol applications. For cells outside of the organism, multiple techniques exist in the art to administer the compounds, including (but not limited to) cell microinjection techniques, transformation techniques and carrier techniques.

[00051] The abnormal condition can also be prevented or treated by administering a compound to a group of cells having an aberration in a signal transduction pathway to an organism. The effect of administering a compound on organism function can then be monitored. The organism is preferably a mouse, rat, rabbit, guinea pig or goat, more preferably a monkey or ape, and most preferably a human.

[00052] By "amplification" it is meant increased numbers of DNA or RNA in a cell compared with normal cells. "Amplification" as it refers to RNA can be the detectablepresence of RNA in cells, since in some normal cells there is no basal expression of RNA. In other normal cells, a

basal level of expression exists, therefore in these cases amplification is the detection of at least 1 to 2-fold, and preferably more, compared to the basal level.

[00053] As used herein, the phrase "stringent hybridization conditions" or "stringent conditions" refers to conditions under which a probe, primer, or oligonucleotide will hybridize to its target sequence, but to no other sequences. Stringent conditions are sequence-dependent and will be different in different circumstances. Longer sequences hybridize specifically at higher temperatures. Generally, stringent conditions are selected to be about 5°C lower than the thermal melting point (T_m) for the specific sequence at a defined ionic strength and pH. The T_m is the temperature (under defined ionic strength, pH and nucleic acid concentration) at which 50% of the probes complementary to the target sequence hybridize to the target sequence at equilibrium. Since the target sequences are generally present in excess, at T_m, 50% of the probes are occupied at equilibrium. Typically, stringent conditions will be those in which the salt concentration is less than about 1.0 M sodium ion, typically about 0.01 to 1.0 M sodium ion (or other salts) at pH 7.0 to 8.3 and the temperature is at least about 30°C for short probes, primers or oligonucleotides (e.g. 10 to 50 nucleotides) and at least about 60°C for longer probes, primers or oligonucleotides. Stringent conditions may also be achieved with the addition of destabilizing agents, such as formamide.

[00054] The amino acid sequences are presented in the amino to carboxy direction, from left to right. The amino and carboxy groups are not presented in the sequence. The nucleotide sequences are presented by single strand only, in the 5' to 3' direction, from left to right. Nucleotides and amino acids are represented in the manner recommended by the IUPAC-IUB Biochemical Nomenclature Commission or (for amino acids) by three letters code.

Polynucleotides

[00055] The present invention provides purified and isolated polynucleotides (*e.g.*, DNA sequences and RNA transcripts, both sense and complementary antisense strands, both single and double-stranded, including splice variants thereof) that encode unknown G protein-coupled receptors heretofore termed novel GPCRs, or nGPCRs. These genes are described herein and designated herein collectively as nGPCR-x (where x is 2227-2229, 2280-2286, 2469-2479, 2480-2489, 2490-2499, 2500-2506, 2507-2516, 2517-2526, 2527-2536, 2537-2548, 2550-2554, 2555-2565, 2566-2576, and 2577-2587). Table 1 below identifies the novel gene sequence nGPCR-x designation, the SEQ ID NO: of the gene sequence, the SEQ ID NO: of the polypeptide encoded thereby, and the U.S. Provisional Application in which the gene sequence has been disclosed.

Table 1

nGPCR	Nucleotide Sequence	Amino acid Sequence	Originally filed in:		nGPCR	Nucleotide Sequence	Amino acid Sequence	Originally filed in:

	(SEQ ID NO:)	(SEQ ID NO:)			(SEQ ID NO:)	(SEQ ID NO:)	
2227	1	129	A	2523	65	193	G
2228	2	130	A	2524	66	194	G
2229	3	131	A	2525	67	195	G
2280	4	132	A	2526	68	196	G
2281	5	133	A	2527	69	197	H
2282	6	134	A	2528	70	198	H
2283	7	135	A	2529	71	199	H
2284	8	136	A	2530	72	200	H
2285	9	137	A	2531	73	201	H
2286	10	138	A	2532	74	202	H
2469	11	139	B	2533	75	203	H
2470	12	140	B	2534	76	204	H
2471	13	141	B	2535	77	205	H
2472	14	142	B	2536	78	206	H
2473	15	143	B	2537	79	207	I
2474	16	144	B	2538	80	208	I
2475	17	145	B	2539	81	209	I
2476	18	146	B	2540	82	210	I
2477	19	147	B	2541	83	211	I
2478	20	148	B	2542	84	212	I
2479	21	149	B	2543	85	213	I
2480	22	150	C	2544	86	214	I
2481	23	151	C	2545	87	215	I
2482	24	152	C	2546	88	216	I
2483	25	153	C	2547	89	217	I
2484	26	154	C	2548	90	218	I
2485	27	155	C	2550	91	219	J
2486	28	156	C	2551	92	220	J
2487	29	157	C	2552	93	221	J
2488	30	158	C	2553	94	222	J
2489	31	159	C	2554	95	223	J
2490	32	160	D	2555	96	224	K
2491	33	161	D	2556	97	225	K
2492	34	162	D	2557	98	226	K
2493	35	163	D	2558	99	227	K
2494	36	164	D	2559	100	228	K
2495	37	165	D	2560	101	229	K
2496	38	166	D	2561	102	230	K
2497	39	167	D	2562	103	231	K
2498	40	168	D	2563	104	232	K
2499	41	169	D	2564	105	233	K
2500	42	170	E	2565	106	234	K
2501	43	171	E	2566	107	235	L
2502	44	172	E	2567	108	236	L
2503	45	173	E	2568	109	237	L
2504	46	174	E	2569	110	238	L
2505	47	175	E	2570	111	239	L
2506	48	176	E	2571	112	240	L
2507	49	177	F	2572	113	241	L
2508	50	178	F	2573	114	242	L
2509	51	179	F	2574	115	243	L
2510	52	180	F	2575	116	244	L
2511	53	181	F	2576	117	245	L
2512	54	182	F	2577	118	246	M
2513	55	183	F	2578	119	247	M
2514	56	184	F	2579	120	248	M
2515	57	185	F	2580	121	249	M
2516	58	186	F	2581	122	250, 251	M
2517	59	187	G	2582	123	252	M
2518	60	188	G	2583	124	253	M
2519	61	189	G	2584	125	254	M
2520	62	190	G	2585	126	255	M
2521	63	191	G	2586	127	256	M
2522	64	192	G	2587	128	257	M

Legend

A= Ser. No. 60/189,783	B= Ser. No. 60/189,918
C= Ser. No. 60/189,960	D= Ser. No. 60/189,917
E= Ser. No. 60/189,907	F= Ser. No. 60/192,945
G= Ser. No. 60/192,916	H= Ser. No. 60/192,923
I= Ser. No. 60/192,933	J= Ser. No. 60/192,830
K= Ser. No. 60/192,234	L= Ser. No. 60/192,155
M= Ser. No. 60/192,935	

[00056] When a specific nGPCR is identified (for example nGPCR-2285), it is understood that only that specific nGPCR is being referred to.

[00057] It is well known that GPCRs are expressed in many different tissues, including thebrain. Accordingly, the nGPCR-x of the present invention may be useful, *inter alia*, for treating and/or diagnosing mental disorders. Following the techniques described in Example 5, below, those skilled in the art could readily ascertain if nGPCR-x is expressed in a particular tissue or region.

[00058] The invention provides purified and isolated polynucleotides (*e.g.*, cDNA, genomic DNA, synthetic DNA, RNA, or combinations thereof, whether single- or double-stranded) that comprise a nucleotide sequence encoding the amino acid sequence of the polypeptides of the invention. Such polynucleotides are useful for recombinantly expressing the receptor and also for detecting expression of the receptor in cells (*e.g.*, using Northern hybridization and *in situ* hybridization assays). Such polynucleotides also are useful in the design of antisense and other molecules for the suppression of the expression of nGPCR-x in a cultured cell, a tissue, or an animal; for therapeutic purposes; or to provide a model for diseases or conditions characterized by aberrant nGPCR-x expression. Specifically excluded from the definition of polynucleotides of the invention are entire isolated, non-recombinant native chromosomes of host cells. A preferred polynucleotide has a sequence selected from the group consisting of SEQ ID NO:1 to SEQ ID NO:128, which correspond to naturally occurring nGPCR-x sequences. It will be appreciated that numerous other polynucleotide sequences exist that also encode nGPCR-x having the sequence selected from the group consisting of SEQ ID NO:129 to SEQ ID NO:257, due to the well-known degeneracy of the universal genetic code.

[00059] The invention also provides a purified and isolated polynucleotide comprising a nucleotide sequence that encodes a mammalian polypeptide, wherein the polynucleotide hybridizes to a polynucleotide having the sequence set forth in sequences selected from the group consisting of SEQ ID NO:1 to SEQ ID NO:128, or the non-coding strand complementary thereto, under the following hybridization conditions:

(a) hybridization for 16 hours at 42°C in a hybridization solution comprising 50% formamide, 1% SDS, 1 M NaCl, 10% dextran sulfate; and

(b) washing 2 times for 30 minutes each at 60°C in a wash solution comprising 0.1% SSC, 1% SDS. Polynucleotides that encode a human allelic variant are highly preferred.

[00060] The present invention relates to molecules which comprise the gene sequences that encode the nGPCRs; constructs and recombinant host cells incorporating the gene sequences; the novel GPCR polypeptides encoded by the gene sequences; antibodies to the polypeptides and homologs; kits employing the polynucleotides and polypeptides, and methods of making and using all of the foregoing. In addition, the present invention relates to homologs of the gene sequences and of the polypeptides and methods of making and using the same.

[00061] Genomic DNA of the invention comprises the protein-coding region for a polypeptide of the invention and is also intended to include allelic variants thereof. It is widely understood that, for many genes, genomic DNA is transcribed into RNA transcripts that undergo one or more splicing events wherein intron (*i.e.*, non-coding regions) of the transcripts are removed, or "spliced out." RNA transcripts that can be spliced by alternative mechanisms, and therefore be subject to removal of different RNA sequences but still encode a nGPCR-x polypeptide, are referred to in the art as splice variants which are embraced by the invention. Splice variants comprehended by the invention therefore are encoded by the same original genomic DNA sequences but arise from distinct mRNA transcripts. Allelic variants are modified forms of a wild-type gene sequence, the modification resulting from recombination during chromosomal segregation or exposure to conditions which give rise to genetic mutation. Allelic variants, like wild type genes, are naturally occurring sequences (as opposed to non-naturally occurring variants that arise from *in vitro* manipulation).

[00062] The invention also comprehends cDNA that is obtained through reverse transcription of an RNA polynucleotide encoding nGPCR-x (conventionally followed by second strand synthesis of a complementary strand to provide a double-stranded DNA).

[00063] Preferred DNA sequences encoding human nGPCR-x polypeptides are selected from the group consisting of SEQ ID NO:1 to SEQ ID NO:128. A preferred DNA of the invention comprises a double stranded molecule along with the complementary molecule (the "non-coding strand" or "complement") having a sequence unambiguously deducible from the coding strand according to Watson-Crick base-pairing rules for DNA. Also preferred are other polynucleotides encoding the nGPCR-x polypeptide selected from the group consisting of SEQ ID NO:129 to SEQ ID NO:257, which differ in sequence from the polynucleotides selected from the group consisting of SEQ ID NO:1 to SEQ ID NO:128, by virtue of the well-known degeneracy of the universal nuclear genetic code.

[00064] The invention further embraces other species, preferably mammalian, homologs of the human nGPCR-x DNA. Species homologs, sometimes referred to as "orthologs," in general, share at least 35%, at least 40%, at least 45%, at least 50%, at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or at least

99% homology with human DNA of the invention. Generally, percent sequence "homology" with respect to polynucleotides of the invention may be calculated as the percentage of nucleotide bases in the candidate sequence that are identical to nucleotides in the nGPCR-x sequence set forth in sequences selected from the group consisting of SEQ ID NO:1 to SEQ ID NO:128, after aligning the sequences and introducing gaps, if necessary, to achieve the maximum percent sequence identity.

[00065] Polynucleotides of the invention permit identification and isolation of polynucleotides encoding related nGPCR-x polypeptides, such as human allelic variants and species homologs, by well-known techniques including Southern and/or Northern hybridization, and polymerase chain reaction (PCR). Examples of related polynucleotides include human and non-human genomic sequences, including allelic variants, as well as polynucleotides encoding polypeptides homologous to nGPCR-x and structurally related polypeptides sharing one or more biological, immunological, and/or physical properties of nGPCR-x. Non-human species genes encoding proteins homologous to nGPCR-x can also be identified by Southern and/or PCR analysis and are useful in animal models for nGPCR-x disorders. Knowledge of the sequence of a human nGPCR-x DNA also makes possible through use of Southern hybridization or polymerase chain reaction (PCR) the identification of genomic DNA sequences encoding nGPCR-x expression control regulatory sequences such as promoters, operators, enhancers, repressors, and the like. Polynucleotides of the invention are also useful in hybridization assays to detect the capacity of cells to express nGPCR-x. Polynucleotides of the invention may also provide a basis for diagnostic methods useful for identifying a genetic alteration(s) in a nGPCR-x locus that underlies a disease state or states, which information is useful both for diagnosis and for selection of therapeutic strategies.

[00066] According to the present invention, the nGPCR-x nucleotide sequences disclosed herein may be used to identify homologs of the nGPCR-x, in other animals, including but not limited to humans and other mammals, and invertebrates. Any of the nucleotide sequences disclosed herein, or any portion thereof, can be used, for example, as probes to screen databases or nucleic acid libraries, such as, for example, genomic or cDNA libraries, to identify homologs, using screening procedures well known to those skilled in the art. Accordingly, homologs having at least 50%, more preferably at least 60%, more preferably at least 70%, more preferably at least 80%, more preferably at least 90%, more preferably at least 95%, and most preferably at least 100% homology with nGPCR-x sequences can be identified.

[00067] The disclosure herein of full-length polynucleotides encoding nGPCR-x polypeptides makes readily available to the worker of ordinary skill in the art every possible fragment of the full-length polynucleotide.

[00068] One preferred embodiment of the present invention provides an isolated nucleic acid molecule comprising a sequence homologous sequences selected from the group consisting of SEQ ID NO:1 to SEQ ID NO:128, and fragments thereof. Another preferred embodiment provides an isolated nucleic acid molecule comprising a sequence selected from the group consisting of SEQ ID NO:1 to SEQ ID NO:128, and fragments thereof.

[00069] As used in the present invention, fragments of nGPCR-x-encoding polynucleotides comprise at least 10, and preferably at least 12, 14, 16, 18, 20, 25, 50, or 75 consecutive nucleotides of a polynucleotide encoding nGPCR-x. Preferably, fragment polynucleotides of the invention comprise sequences unique to the nGPCR-x-encoding polynucleotide sequence, and therefore hybridize under highly stringent or moderately stringent conditions only (*i.e.*, "specifically") to polynucleotides encoding nGPCR-x (or fragments thereof). Polynucleotide fragments of genomic sequences of the invention comprise not only sequences unique to the coding region, but also include fragments of the full-length sequence derived from introns, regulatory regions, and/or other non-translated sequences. Sequences unique to polynucleotides of the invention are recognizable through sequence comparison to other known polynucleotides, and can be identified through use of alignment programs routinely utilized in the art, *e.g.*, those made available in public sequence databases. Such sequences also are recognizable from Southern hybridization analyses to determine the number of fragments of genomic DNA to which a polynucleotide will hybridize. Polynucleotides of the invention can be labeled in a manner that permits their detection, including radioactive, fluorescent, and enzymatic labeling.

[00070] Fragment polynucleotides are particularly useful as probes for detection of full-length or fragments of nGPCR-x polynucleotides. One or more polynucleotides can be included in kits that are used to detect the presence of a polynucleotide encoding nGPCR-x, or used to detect variations in a polynucleotide sequence encoding nGPCR-x.

[00071] The invention also embraces DNAs encoding nGPCR-x polypeptides that hybridize under moderately stringent or high stringency conditions to the non-coding strand, or complement, of the polynucleotides set forth in sequences selected from the group consisting of SEQ ID NO:1 to SEQ ID NO:128.

[00072] Exemplary highly stringent hybridization conditions are as follows: hybridization at 42°C in a hybridization solution comprising 50% formamide, 1% SDS, 1 M NaCl, 10% Dextran sulfate, and washing twice for 30 minutes at 60°C in a wash solution comprising 0.1X SSC and 1% SDS. It is understood in the art that conditions of equivalent stringency can be achieved through variation of temperature and buffer, or salt concentration as described Ausubel *et al.* (Eds.), Protocols in Molecular Biology, John Wiley & Sons (1994), pp. 6.0.3 to 6.4.10. Modifications in hybridization conditions can be empirically determined or precisely calculated

based on the length and the percentage of guanosine/cytosine (GC) base pairing of the probe. The hybridization conditions can be calculated as described in Sambrook, *et al.*, (Eds.), Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratory Press: Cold Spring Harbor, New York (1989), pp. 9.47 to 9.51.

[00073] With the knowledge of the nucleotide sequence information disclosed in the present invention, one skilled in the art can identify and obtain nucleotide sequences which encode nGPCR-x from different sources (*i.e.*, different tissues or different organisms) through a variety of means well known to the skilled artisan and as disclosed by, for example, Sambrook et al., "Molecular cloning: a laboratory manual", Second Edition, Cold Spring Harbor Press, Cold Spring Harbor, NY (1989), which is incorporated herein by reference in its entirety.

[00074] For example, DNA that encodes nGPCR-x may be obtained by screening of mRNA, cDNA, or genomic DNA with oligonucleotide probes generated from the nGPCR-x gene sequence information provided herein. Probes may be labeled with a detectable group, such as a fluorescent group, a radioactive atom or a chemiluminescent group in accordance with procedures known to the skilled artisan and used in conventional hybridization assays, as described by, for example, Sambrook *et al.*

[00075] A nucleic acid molecule comprising any of the nGPCR-x nucleotide sequences described above can alternatively be synthesized by use of the polymerase chain reaction (PCR) procedure, with the PCR oligonucleotide primers produced from the nucleotide sequences provided herein. See U.S. Patent Numbers 4,683,195 to Mullis *et al.* and 4,683,202 to Mullis. The PCR reaction provides a method for selectively increasing the concentration of a particular nucleic acid sequence even when that sequence has not been previously purified and is present only in a single copy in a particular sample. The method can be used to amplify either single or double-stranded DNA. The essence of the method involves the use of two oligonucleotide probes to serve as primers for the template-dependent, polymerase mediated replication of a desired nucleic acid molecule.

[00076] A wide variety of alternative cloning and *in vitro* amplification methodologies are well known to those skilled in the art. Examples of these techniques are found in, for example, Berger *et al.*, *Guide to Molecular Cloning Techniques*, Methods in Enzymology 152, Academic Press, Inc., San Diego, CA (Berger), which is incorporated herein by reference in its entirety.

[00077] Automated sequencing methods can be used to obtain or verify the nucleotide sequence of nGPCR-x. The nGPCR-x nucleotide sequences of the present invention are believed to be 100% accurate. However, as is known in the art, nucleotide sequence obtained by automated methods may contain some errors. Nucleotide sequences determined by automation are typically at least about 90%, more typically at least about 95% to at least about 99.9% identical

to the actual nucleotide sequence of a given nucleic acid molecule. The actual sequence may be more precisely determined using manual sequencing methods, which are well known in the art. An error in a sequence which results in an insertion or deletion of one or more nucleotides may result in a frame shift in translation such that the predicted amino acid sequence will differ from that which would be predicted from the actual nucleotide sequence of the nucleic acid molecule, starting at the point of the mutation.

[00078] The nucleic acid molecules of the present invention, and fragments derived therefrom, are useful for screening for restriction fragment length polymorphism (RFLP) associated with certain disorders, as well as for genetic mapping.

[00079] The polynucleotide sequence information provided by the invention makes possible large-scale expression of the encoded polypeptide by techniques well known and routinely practiced in the art.

Vectors

[00080] Another aspect of the present invention is directed to vectors, or recombinant expression vectors, comprising any of the nucleic acid molecules described above. Vectors are used herein either to amplify DNA or RNA encoding nGPCR-x and/or to express DNA which encodes nGPCR-x. Preferred vectors include, but are not limited to, plasmids, phages, cosmids, episomes, viral particles or viruses, and integratable DNA fragments (*i.e.*, fragments integratable into the host genome by homologous recombination). Preferred viral particles include, but are not limited to, adenoviruses, baculoviruses, parvoviruses, herpesviruses, poxviruses, adeno-associated viruses, Semliki Forest viruses, vaccinia viruses, and retroviruses. Preferred expression vectors include, but are not limited to, pcDNA3 (Invitrogen) and pSVL (Pharmacia Biotech). Other expression vectors include, but are not limited to, pSPORT™ vectors, pGEM™ vectors (Promega), pPROEXvectors™ (LTI, Bethesda, MD), Bluescript™ vectors (Stratagene), pQE™ vectors (Qiagen), pSE420™ (Invitrogen), and pYES2™(Invitrogen).

[00081] Expression constructs preferably comprise GPCR-x-encoding polynucleotides operatively linked to an endogenous or exogenous expression control DNA sequence and a transcription terminator. Expression control DNA sequences include promoters, enhancers, operators, and regulatory element binding sites generally, and are typically selected based on the expression systems in which the expression construct is to be utilized. Preferred promoter and enhancer sequences are generally selected for the ability to increase gene expression, while operator sequences are generally selected for the ability to regulate gene expression. Expression constructs of the invention may also include sequences encoding one or more selectable markers that permit identification of host cells bearing the construct. Expression constructs may also include sequences that facilitate, and preferably promote, homologous recombination in a host

cell. Preferred constructs of the invention also include sequences necessary for replication in a host cell.

[00082] Expression constructs are preferably utilized for production of an encoded protein, but may also be utilized simply to amplify a nGPCR-x-encoding polynucleotide sequence. In preferred embodiments, the vector is an expression vector wherein the polynucleotide of the invention is operatively linked to a polynucleotide comprising an expression control sequence. Autonomously replicating recombinant expression constructs such as plasmid and viral DNA vectors incorporating polynucleotides of the invention are also provided. Preferred expression vectors are replicable DNA constructs in which a DNA sequence encoding nGPCR-x is operably linked or connected to suitable control sequences capable of effecting the expression of the nGPCR-x in a suitable host. DNA regions are operably linked or connected when they are functionally related to each other. For example, a promoter is operably linked or connected to a coding sequence if it controls the transcription of the sequence. Amplification vectors do not require expression control domains, but rather need only the ability to replicate in a host, usually conferred by an origin of replication, and a selection gene to facilitate recognition of transformants. The need for control sequences in the expression vector will vary depending upon the host selected and the transformation method chosen. Generally, control sequences include a transcriptional promoter, an optional operator sequence to control transcription, a sequence encoding suitable mRNA ribosomal binding and sequences which control the termination of transcription and translation.

[00083] Preferred vectors preferably contain a promoter that is recognized by the host organism. The promoter sequences of the present invention may be prokaryotic, eukaryotic or viral. Examples of suitable prokaryotic sequences include the P_R and P_L promoters of bacteriophage lambda (The bacteriophage Lambda, Hershey, A. D., Ed., Cold Spring Harbor Press, Cold Spring Harbor, NY (1973), which is incorporated herein by reference in its entirety; Lambda II, Hendrix, R. W., Ed., Cold Spring Harbor Press, Cold Spring Harbor, NY (1980), which is incorporated herein by reference in its entirety); the trp, recA, heat shock, and lacZ promoters of *E. coli* and the SV40 early promoter (Benoist *et al. Nature*, 1981, *290*, 304-310, which is incorporated herein by reference in its entirety). Additional promoters include, but are not limited to, mouse mammary tumor virus, long terminal repeat of human immunodeficiency virus, maloney virus, cytomegalovirus immediate early promoter, Epstein Barr virus, Rous sarcoma virus, human actin, human myosin, human hemoglobin, human muscle creatine, and human metalothionein.

[00084] Additional regulatory sequences can also be included in preferred vectors. Preferred examples of suitable regulatory sequences are represented by the Shine-Dalgarno of the

replicase gene of the phage MS-2 and of the gene cII of bacteriophage lambda. The Shine-Dalgarno sequence may be directly followed by DNA encoding nGPCR-x and result in the expression of the mature nGPCR-x protein.

[00085] Moreover, suitable expression vectors can include an appropriate marker that allows the screening of the transformed host cells. The transformation of the selected host is carried out using any one of the various techniques well known to the expert in the art and described in Sambrook *et al.*, *supra*.

[00086] An origin of replication can also be provided either by construction of the vector to include an exogenous origin or may be provided by the host cell chromosomal replication mechanism. If the vector is integrated into the host cell chromosome, the latter may be sufficient. Alternatively, rather than using vectors which contain viral origins of replication, one skilled in the art can transform mammalian cells by the method of co-transformation with a selectable marker and nGPCR-x DNA. An example of a suitable marker is dihydrofolate reductase (DHFR) or thymidine kinase (*see*, U.S. Patent No. 4,399,216).

[00087] Nucleotide sequences encoding GPCR-x may be recombined with vector DNA in accordance with conventional techniques, including blunt-ended or staggered-ended termini for ligation, restriction enzyme digestion to provide appropriate termini, filling in of cohesive ends as appropriate, alkaline phosphatase treatment to avoid undesiderable joining, and ligation with appropriate ligases. Techniques for such manipulation are disclosed by Sambrook et al.,*supra* and are well known in the art. Methods for construction of mammalian expression vectors are disclosed in, for example, Okayama *et al.*, *Mol. Cell. Biol.*, **1983**,*3*, 280, Cosman *et al.*, *Mol. Immunol.*, **1986**, *23*, 935, Cosman *et al.*, *Nature*, **1984**, *312*, 768, EP-A-0367566, and WO 91/18982, each of which is incorporated herein by reference in its entirety.

Host cells

[00088] According to another aspect of the invention, host cells are provided, induding prokaryotic and eukaryotic cells, comprising a polynucleotide of the invention (or vector of the invention) in a manner that permits expression of the encoded nGPCR-x polypeptide. Polynucleotides of the invention may be introduced into the host cell as part of a circular plasmid, or as linear DNA comprising an isolated protein coding region or a viral vector. Methods for introducing DNA into the host cell that are well known and routinely practiced in the art include transformation, transfection, electroporation, nuclear injection, or fusion with carriers such as liposomes, micelles, ghost cells, and protoplasts. Expression systems of the invention include bacterial, yeast, fungal, plant, insect, invertebrate, vertebrate, and mammalian cells systems.

[00089] The invention provides host cells that are transformed or transfected (stably or transiently) with polynucleotides of the invention or vectors of the invention. As stated above, such host cells are useful for amplifying the polynucleotides and also for expressing the nGPCR-x polypeptide or fragment thereof encoded by the polynucleotide.

[00090] In still another related embodiment, the invention provides a method for producing a nGPCR-x polypeptide (or fragment thereof) comprising the steps of growing a host cell of the invention in a nutrient medium and isolating the polypeptide or variant thereof from the cell or the medium. Because nGPCR-x is a seven transmembrane receptor, it will be appreciated that, for some applications, such as certain activity assays, the preferable isolation may involve isolation of cell membranes containing the polypeptide embedded therein, whereas for other applications a more complete isolation may be preferable.

[00091] According to some aspects of the present invention, transformed host cells having an expression vector comprising any of the nucleic acid molecules described above are provided. Expression of the nucleotide sequence occurs when the expression vector is introduced into an appropriate host cell. Suitable host cells for expression of the polypeptides of the invention include, but are not limited to, prokaryotes, yeast, and eukaryotes. If a prokaryotic expression vector is employed, then the appropriate host cell would be any prokaryotic cell capable of expressing the cloned sequences. Suitable prokaryotic cells include, but are not limited to, bacteria of the genera *Escherichia*, *Bacillus*, *Salmonella*, *Pseudomonas*, *Streptomyces*, and *Staphylococcus*.

[00092] If an eukaryotic expression vector is employed, then the appropriate host cell would be any eukaryotic cell capable of expressing the cloned sequence. Preferably, eukaryotic cells are cells of higher eukaryotes. Suitable eukaryotic cells include, but are not limited to, non-human mammalian tissue culture cells and human tissue culture cells. Preferred host cells include, but are not limited to, insect cells, HeLa cells, Chinese hamster ovary cells (CHO cells), African green monkey kidney cells (COS cells), human HEK-293 cells, and murine 3T3 fibroblasts. Propagation of such cells in cell culture has become a routine procedure (*see*, Tissue Culture, Academic Press, Kruse and Patterson, eds. (1973), which is incorporated herein by reference in its entirety).

[00093] In addition, a yeast host may be employed as a host cell. Preferred yeast cells include, but are not limited to, the genera *Saccharomyces*, *Pichia*, and *Kluveromyces*. Preferred yeast hosts are *S. cerevisiae* and *P. pastoris*. Preferred yeast vectors can contain an origin of replication sequence from a 2T yeast plasmid, an autonomously replication sequence (ARS), a promoter region, sequences for polyadenylation, sequences for transcription termination, and a

selectable marker gene. Shuttle vectors for replication in both yeast and *E. coli* are also included herein.

[00094] Alternatively, insect cells may be used as host cells. In a preferred embodiment, the polypeptides of the invention are expressed using a baculovirus expression system (*see*, Luckow *et al.*, *Bio/Technology*, **1988**, *6*, 47, Baculovirus Expression Vectors: A Laboratory Manual, O'Rielly *et al.* (Eds.), W.H. Freeman and Company, New York, **1992**, and U.S. Patent No. 4,879,236, each of which is incorporated herein by reference in its entirety). In addition, the MAXBAC™ complete baculovirus expression system (Invitrogen) can, for example, be used for production in insect cells.

[00095] Host cells of the invention are a valuable source of immunogen for development of antibodies specifically immunoreactive with nGPCR-x. Host cells of the invention are also useful in methods for the large-scale production of nGPCR-x polypeptides wherein the cells are grown in a suitable culture medium and the desired polypeptide products are isolated from the cells, or from the medium in which the cells are grown, by purification methods known in the art, *e.g.*, conventional chromatographic methods including immunoaffinity chromatography, receptor affinity chromatography, hydrophobic interaction chromatography, lectin affinity chromatography, size exclusion filtration, cation or anion exchange chromatography, high pressure liquid chromatography (HPLC), reverse phase HPLC, and the like. Still other methods of purification include those methods wherein the desired protein is expressed and purified as a fusion protein having a specific tag, label, or chelating moiety that is recognized by a specific binding partner or agent. The purified protein can be cleaved to yield the desired protein, or can be left as an intact fusion protein. Cleavage of the fusion component may produce a form of the desired protein having additional amino acid residues as a result of the cleavage process.

[00096] Knowledge of nGPCR-x DNA sequences allows for modification of cells to permit, or increase, expression of endogenous nGPCR-x. Cells can be modified (*e.g.*, by homologous recombination) to provide increased expression by replacing, in whole or in part, the naturally occurring nGPCR-x promoter with all or part of a heterologous promoter so that the cells express nGPCR-x at higher levels. The heterologous promoter is inserted in such a manner that it is operatively linked to endogenous nGPCR-x encoding sequences. (See, for example, PCT International Publication No. WO 94/12650, PCT International Publication No. WO 92/20808, and PCT International Publication No. WO 91/09955.) It is also contemplated that, in addition to heterologous promoter DNA, amplifiable marker DNA (*e.g.*, ada, dhfr, and the multifunctional CAD gene which encodes carbamoyl phosphate synthase, aspartate transcarbamylase, and dihydroorotase) and/or intron DNA may be inserted along with the heterologous promoter DNA. If linked to the nGPCR-x coding sequence, amplification of the

marker DNA by standard selection methods results in co-amplification of the nGPCR-x coding sequences in the cells.

Knock-outs

[00097] The DNA sequence information provided by the present invention also makes possible the development (*e.g.*, by homologous recombination or "knock-out" strategies; see Capecchi, *Science 244*:1288-1292 (1989), which is incorporated herein by reference) of animals that fail to express functional nGPCR-x or that express a variant of nGPCR-x. Such animals (especially small laboratory animals such as rats, rabbits, and mice) are useful as models for studying the*in vivo* activities of nGPCR-x and modulators of nGPCR-x.

Antisense

[00098] Also made available by the invention are anti-sense polynucleotides that recognize and hybridize to polynucleotides encoding nGPCR-x. Full-length and fragment anti-sense polynucleotides are provided. Fragment antisense molecules of the invention include (i) those that specifically recognize and hybridize to nGPCR-x RNA (as determined by sequence comparison of DNA encoding nGPCR-x to DNA encoding other known molecules). Identification of sequences unique to nGPCR-x encoding polynucleotides can be deduced through use of any publicly available sequence database, and/or through use of commercially available sequence comparison programs. After identification of the desired sequences, isolation through restriction digestion or amplification using any of the various polymerase chain reaction techniques well known in the art can be performed. Anti-sense polynucleotides are particularly relevant to regulating expression of nGPCR-x by those cells expressing nGPCR-x mRNA.

[00099] Antisense nucleic acids (preferably 10 to 30 base-pair oligonucleotides) capable of specifically binding to nGPCR-x expression control sequences or nGPCR-x RNA are introduced into cells (*e.g.*, by a viral vector or colloidal dispersion system such as a liposome). The antisense nucleic acid binds to the nGPCR-x target nucleotide sequence in the cell and prevents transcription and/or translation of the target sequence. Phosphorothioate and methylphosphonate antisense oligonucleotides are specifically contemplated for therapeutic use by the invention. The antisense oligonucleotides may be further modified by adding poly-L-lysine, transferrin polylysine, or cholesterol moieties at their 5' end. Suppression of nGPCR-x expression at either the transcriptional or translational level is useful to generate cellular or animal models for diseases/conditions characterized by aberrant nGPCR-x expression.

[000100] Antisense oligonucleotides, or fragments of sequences selected from the group consisting of SEQ ID NO:1 to SEQ ID NO:128, or sequences complementary or homologous thereto, derived from the nucleotide sequences of the present invention encoding nGPCR-x are

useful as diagnostic tools for probing gene expression in various tissues. For example, tissue can be probed *in situ* with oligonucleotide probes carrying detectable groups by conventional autoradiography techniques to investigate native expression of this enzyme or pathological conditions relating thereto. Antisense oligonucleotides are preferably directed to regulatory regions of sequences selected from the group consisting of SEQ ID NO:1 to SEQ ID NO:128, or mRNA corresponding thereto, including, but not limited to, the initiation codon, TATA box, enhancer sequences, and the like.

Transcription factors

[000101] The nGPCR-x sequences taught in the present invention facilitate the design of novel transcription factors for modulating nGPCR-x expression in native cells and animals, and cells transformed or transfected with nGPCR-x polynucleotides. For example, the Cys_2-His_2 zinc finger proteins, which bind DNA via their zinc finger domains, have been shown to be amenable to structural changes that lead to the recognition of different target sequences. These artificial zinc finger proteins recognize specific target sites with high affinity and low dissociation constants, and are able to act as gene switches to modulate gene expression. Knowledge of the particular nGPCR-x target sequence of the present invention facilitates the engineering of zinc finger proteins specific for the target sequence using known methods such as a combination of structure-based modeling and screening of phage display libraries (Segal *et al.*, Proc. Natl. Acad. Sci. (USA) 96:2758-2763 (1999); Liu *et al.*, Proc. Natl. Acad. Sci. (USA) 94:5525-5530 (1997); Greisman *et al.*, Science 275:657-661 (1997); Choo *et al.*, J. Mol. Biol. 273:525-532 (1997)). Each zinc finger domain usually recognizes three or more base pairs. Since a recognition sequence of 18 base pairs is generally sufficient in length to render it unique in any known genome, a zinc finger protein consisting of 6 tandem repeats of zinc fingers would be expected to ensure specificity for a particular sequence (Segal *et al.*) The artificial zinc finger repeats, designed based on nGPCR-x sequences, are fused to activation or repression domains to promote or suppress nGPCR-x expression (Liu *et al.)* Alternatively, the zinc finger domains can be fused to the TATA box-binding factor (TBP) with varying lengths of linker region between the zinc finger peptide and the TBP to create either transcriptional activators or repressors (Kim *et al.*, Proc. Natl. Acad. Sci. (USA) 94:3616-3620 (1997). Such proteins and polynucleotides that encode them, have utility for modulating nGPCR-x expression *in vivo* in both native cells, animals and humans; and/or cells transfected with nGPCR-x-encoding sequences. The novel transcription factor can be delivered to the target cells by transfecting constructs that express the transcription factor (gene therapy), or by introducing the protein. Engineered zinc finger proteins can also be designed to bind RNA sequences for use in therapeutics as alternatives to antisense or catalytic RNA methods (McColl *et al.*, Proc. Natl. Acad. Sci. (USA) 96:9521-9526

(1997); Wu *et al.*, Proc. Natl. Acad. Sci. (USA) 92:344-348 (1995)). The present invention contemplates methods of designing such transcription factors based on the gene sequence of the invention, as well as customized zinc finger proteins, that are useful to modulate nGPCR-x expression in cells (native or transformed) whose genetic complement includes these sequences.

Polypeptides

[000102] The invention also provides purified and isolated mammalian nGPCR-x polypeptides encoded by a polynucleotide of the invention. Presently preferred is a human nGPCR-x polypeptide comprising the amino acid sequence set out in sequences selected from the group consisting of SEQ ID NO:129 to SEQ ID NO:257, or fragments thereof comprising an epitope specific to the polypeptide. By "epitope specific to" is meant a portion of the nGPCR receptor that is recognizable by an antibody that is specific for the nGPCR, as defined in detail below.

[000103] Although the sequences provided are particular human sequences, the invention is intended to include within its scope other human allelic variants; non-human mammalian forms of nGPCR-x, and other vertebrate forms of nGPCR-x.

[000104] It will be appreciated that extracellular epitopes are particularly useful for generating and screening for antibodies and other binding compounds that bind to receptors such as nGPCR-x. Thus, in another preferred embodiment, the invention provides a purified and isolated polypeptide comprising at least one extracellular domain (*e.g.*, the N-terminal extracellular domain or one of the three extracellular loops) of nGPCR-x. Purified and isolated polypeptides comprising the N-terminal extracellular domain of nGPCR-x are highly preferred. Also preferred is a purified and isolated polypeptide comprising a nGPCR-x fragment selected from the group consisting of the N-terminal extracellular domain of nGPCR-x, transmembrane domains of nGPCR-x, an extracellular loop connecting transmembrane domains of nGPCR-x, an intracellular loop connecting transmembrane domains of nGPCR-x, the C-terminal cytoplasmic region of nGPCR-x, and fusions thereof. Such fragments may be continuous portions of the native receptor. However, it will also be appreciated that knowledge of the nGPCR-x gene and protein sequences as provided herein permits recombining of various domains that are not contiguous in the native protein. Using a FORTRAN computer program called "tmtrest.all" [Parodi *et al.*, Comput. Appl. Biosci. 5:527-535 (1994)], nGPCR-x was shown to contain transmembrane-spanning domains.

[000105] The invention also embraces polypeptides that have at least 99%, at least 95%, at least 90%, at least 85%, at least 80%, at least 75%, at least 70%, at least 65%, at least 60%, at least 55% or at least 50% identity and/or homology to the preferred polypeptide of the invention. Percent amino acid sequence "identity" with respect to the preferred polypeptide of the invention is defined herein as the percentage of amino acid residues in the candidate sequence

that are identical with the residues in the nGPCR-x sequence after aligning both sequences and introducing gaps, if necessary, to achieve the maximum percent sequence identity, and not considering any conservative substitutions as part of the sequence identity. Percent sequence "homology" with respect to the preferred polypeptide of the invention is defined herein as the percentage of amino acid residues in the candidate sequence that are identical with the residues in the nGPCR-x sequence after aligning the sequences and introducing gaps, if necessary, to achieve the maximum percent sequence identity, and also considering any conservative substitutions as part of the sequence identity.

[000106] In one aspect, percent homology is calculated as the percentage of amino acid residues in the smaller of two sequences which align with identical amino acid residue in the sequence being compared, when four gaps in a length of 100 amino acids may be introduced to maximize alignment (Dayhoff, in Atlas of Protein Sequence and Structure, Vol. 5, p. 124, National Biochemical Research Foundation, Washington, D.C. (1972), incorporated herein by reference).

[000107] Polypeptides of the invention may be isolated from natural cell sources or may be chemically synthesized, but are preferably produced by recombinant procedures involving host cells of the invention. Use of mammalian host cells is expected to provide for such post-translational modifications (*e.g.*, glycosylation, truncation, lipidation, and phosphorylation) as may be needed to confer optimal biological activity on recombinant expression products of the invention. Glycosylated and non-glycosylated forms of nGPCR-x polypeptides are embraced by the invention.

[000108] The invention also embraces variant (or analog) nGPCR-x polypeptides. In one example, insertion variants are provided wherein one or more amino acid residues supplement a nGPCR-x amino acid sequence. Insertions may be located at either or both termini of the protein, or may be positioned within internal regions of the nGPCR-x amino acid sequence. Insertional variants with additional residues at either or both termini can include, for example, fusion proteins and proteins including amino acid tags or labels.

[000109] Insertion variants include nGPCR-x polypeptides wherein one or more amino acid residues are added to a nGPCR-x acid sequence or to a biologically active fragment thereof.

[000110] Variant products of the invention also include mature nGPCR-x products, *i.e.*, nGPCR-x products wherein leader or signal sequences are removed, with additional amino terminal residues. The additional amino terminal residues may be derived from another protein, or may include one or more residues that are not identifiable as being derived from specific proteins. nGPCR-x products with an additional methionine residue at position -1 (Met^{-1}-nGPCR-x) are contemplated, as are variants with additional methionine and lysine residues at positions -2 and -1 (Met^{-2}-Lys^{-1}-nGPCR-x). Variants of nGPCR-x with additional Met, Met-Lys, Lys residues

(or one or more basic residues in general) are particularly useful for enhanced recombinant protein production in bacterial host cells.

[000111] The invention also embraces nGPCR-x variants having additional amino acid residues that result from use of specific expression systems. For example, use of commercially available vectors that express a desired polypeptide as part of a glutathione-S-transferase (GST) fusion product provides the desired polypeptide having an additional glycine residue at position -1 after cleavage of the GST component from the desired polypeptide. Variants that result from expression in other vector systems are also contemplated.

[000112] Insertional variants also include fusion proteins wherein the amino terminus and/or the carboxy terminus of nGPCR-x is/are fused to another polypeptide.

[000113] In another aspect, the invention provides deletion variants wherein one or more amino acid residues in a nGPCR-x polypeptide are removed. Deletions can be effected at one or both termini of the nGPCR-x polypeptide, or with removal of one or more non-terminal amino acid residues of nGPCR-x. Deletion variants, therefore, include all fragments of a nGPCR-x polypeptide.

[000114] The invention also embraces polypeptide fragments of sequences selected from the group consisting of SEQ ID NO:129 to SEQ ID NO:257, wherein the fragments maintain biological (*e.g.*, ligand binding and/or intracellular signaling) immunological properties of a nGPCR-x polypeptide.

[000115] In one preferred embodiment of the invention, an isolated nucleic acid molecule comprises a nucleotide sequence that encodes a polypeptide comprising an amino acid sequence homologous to sequences selected from the group consisting of SEQ ID NO:129 to SEQ ID NO:257, and fragments thereof, wherein the nucleic acid molecule encoding at least a portion of nGPCR-x. In a more preferred embodiment, the isolated nucleic acid molecule comprises a sequence that encodes a polypeptide comprising sequences selected from the group consisting of SEQ ID NO:129 to SEQ ID NO:257, and fragments thereof.

[000116] As used in the present invention, polypeptide fragments comprise at least 5, 10, 15, 20, 25, 30, 35, or 40 consecutive amino acids of sequences selected from the group consisting of SEQ ID NO:129 to SEQ ID NO:257. Preferred polypeptide fragments display antigenic properties unique to, or specific for, human nGPCR-x and its allelic and species homologs. Fragments of the invention having the desired biological and immunological properties can be prepared by any of the methods well known and routinely practiced in the art.

[000117] In still another aspect, the invention provides substitution variants of nGPCR-x polypeptides. Substitution variants include those polypeptides wherein one or more amino acid residues of a nGPCR-x polypeptide are removed and replaced with alternative residues. In one

aspect, the substitutions are conservative in nature; however, the invention embraces substitutions that are also non-conservative. Conservative substitutions for this purpose may be defined as set out in Tables 2, 3, or 4 below.

[000118] Variant polypeptides include those wherein conservative substitutions have been introduced by modification of polynucleotides encoding polypeptides of the invention. Amino acids can be classified according to physical properties and contribution to secondary and tertiary protein structure. A conservative substitution is recognized in the art as a substitution of one amino acid for another amino acid that has similar properties. Exemplary conservative substitutions are set out in Table 2 (from WO 97/09433, page 10, published March 13, 1997 (PCT/GB96/02197, filed 9/6/96), immediately below.

Table 2

Conservative Substitutions I

SIDE CHAIN CHARACTERISTIC	AMINO ACID
Aliphatic	
Non-polar	G A P I L V
Polar - uncharged	C S T M N Q
Polar - charged	D E K R
Aromatic	H F W Y
Other	N Q D E

[000119] Alternatively, conservative amino acids can be grouped as described in Lehninger, [Biochemistry, Second Edition; Worth Publishers, Inc. NY, NY (1975), pp.71-77] as set out in Table 3, below.

Table 3
Conservative Substitutions II

SIDE CHAIN CHARACTERISTIC	AMINO ACID
Non-polar (hydrophobic)	
A. Aliphatic:	A L I V P
B. Aromatic:	F W
C. Sulfur-containing:	M
D. Borderline:	G
Uncharged-polar	
A. Hydroxyl:	S T Y
B. Amides:	N Q
C. Sulfhydryl:	C
D. Borderline:	G
Positively Charged (Basic):	K R H
Negatively Charged (Acidic):	D E

[000120] As still another alternative, exemplary conservative substitutions are set out in Table 4, below.

Table 4

Conservative Substitutions III

Original Residue	Exemplary Substitution
Ala (A)	Val, Leu, Ile
Arg (R)	Lys, Gln, Asn
Asn (N)	Gln, His, Lys, Arg
Asp (D)	Glu
Cys (C)	Ser
Gln (Q)	Asn
Glu (E)	Asp
His (H)	Asn, Gln, Lys, Arg
Ile (I)	Leu, Val, Met, Ala, Phe,
Leu (L)	Ile, Val, Met, Ala, Phe
Lys (K)	Arg, Gln, Asn
Met (M)	Leu, Phe, Ile
Phe (F)	Leu, Val, Ile, Ala
Pro (P)	Gly
Ser (S)	Thr
Thr (T)	Ser
Trp (W)	Tyr
Tyr (Y)	Trp, Phe, Thr, Ser
Val (V)	Ile, Leu, Met, Phe, Ala

[000121] It should be understood that the definition of polypeptides of the invention is intended to include polypeptides bearing modifications other than insertion, deletion, or substitution of amino acid residues. By way of example, the modifications may be covalent in nature, and include for example, chemical bonding with polymers, lipids, other organic, and inorganic moieties. Such derivatives may be prepared to increase circulating half-life of a polypeptide, or may be designed to improve the targeting capacity of the polypeptide for desired cells, tissues, or organs. Similarly, the invention further embraces nGPCR-x polypeptides that have been covalently modified to include one or more water-soluble polymer attachments such as polyethylene glycol, polyoxyethylene glycol, or polypropylene glycol. Variants that display ligand binding properties of native nGPCR-x and are expressed at higher levels, as well as variants that provide for constitutively active receptors, are particularly useful in assays of the invention; the variants are also useful in providing cellular, tissue and animal models of diseases/conditions characterized by aberrant nGPCR-x activity.

[000122] In a related embodiment, the present invention provides compositions comprising purified polypeptides of the invention. Preferred compositions comprise, in addition to the polypeptide of the invention, a pharmaceutically acceptable (*i.e.*, sterile and non-toxic) liquid, semisolid, or solid diluent that serves as a pharmaceutical vehicle, excipient, or medium. Any diluent known in the art may be used. Exemplary diluents include, but are not limited to, water, saline solutions, polyoxyethylene sorbitan monolaurate, magnesium stearate, methyl-and

propylhydroxybenzoate, talc, alginates, starches, lactose, sucrose, dextrose, sorbitol, mannitol, glycerol, calcium phosphate, mineral oil, and cocoa butter.

[000123] Variants that display ligand binding properties of native nGPCR-x and are expressed at higher levels, as well as variants that provide for constitutively active receptors, are particularly useful in assays of the invention; the variants are also useful in assays of the invention and in providing cellular, tissue and animal models of diseases/conditions characterized by aberrant nGPCR-x activity.

[000124] The G protein-coupled receptor functions through a specific heterotrimeric guanine-nucleotide-binding regulatory protein (G-protein) coupled to the intracellular portion of the G protein-coupled receptor molecule. Accordingly, the G protein-coupled receptor has a specific affinity to G protein. G proteins specifically bind to guanine nucleotides. Isolation of G proteins provides a means to isolate guanine nucleotides. G proteins may be isolated using commercially available anti-G protein antibodies or isolated G protein-coupled receptors. Similarly, G proteins may be detected in a sample isolated using commercially available detectable anti-G protein antibodies or isolated G protein-coupled receptors.

[000125] According to the present invention, the isolated nGPCR-x proteins of the present invention are useful to isolate and purify G proteins from samples such as cell lysates. Example 15 below sets forth an example of isolation of G proteins using isolated nGPCR-x proteins. Such methodolgy may be used in place of the use of commercially available anti-G protein antibodies which are used to isolate G proteins. Moreover, G proteins may be detected using n-GPCR-x proteins in place of commercially available detectable anti-G protein antibodies. Since nGPCR-x proteins specifically bind to G proteins, they can be employed in any specific use where G protein specific affinity is required such as those uses where commercially available anti-G protein antibodies are employed.

Antibodies

[000126] Also comprehended by the present invention are antibodies (*e.g.*, monoclonal and polyclonal antibodies, single chain antibodies, chimeric antibodies, bifunctional/bispecific antibodies, humanized antibodies, human antibodies, and complementary determining region (CDR)-grafted antibodies, including compounds which include CDR sequences which specifically recognize a polypeptide of the invention) specific for nGPCR-x or fragments thereof. Preferred antibodies of the invention are human antibodies that are produced and identified according to methods described in WO93/11236, published June 20, 1993, which is incorporated herein by reference in its entirety. Antibody fragments, including Fab, Fab′, $F(ab')_2$, and F_v, are also provided by the invention. The term "specific for," when used to describe antibodies of the invention, indicates that the variable regions of the antibodies of the

invention recognize and bind nGPCR-x polypeptides exclusively (*i.e.*, are able to distinguish nGPCR-x polypeptides from other known GPCR polypeptides by virtue of measurable differences in binding affinity, despite the possible existence of localized sequence identity, homology, or similarity between nGPCR-x and such polypeptides). It will be understood that specific antibodies may also interact with other proteins (for example, *S. aureus* protein A or other antibodies in ELISA techniques) through interactions with sequences outside the variable region of the antibodies, and, in particular, in the constant region of the molecule. Screening assays to determine binding specificity of an antibody of the invention are well known and routinely practiced in the art. For a comprehensive discussion of such assays, see Harlow*et al.* (Eds.), Antibodies A Laboratory Manual; Cold Spring Harbor Laboratory; Cold Spring Harbor, NY (1988), Chapter 6. Antibodies that recognize and bind fragments of the nGPCR-x polypeptides of the invention are also contemplated, provided that the antibodies are specific for nGPCR-x polypeptides. Antibodies of the invention can be produced using any method well known and routinely practiced in the art.

[000127] The invention provides an antibody that is specific for the nGPCR-x of the invention. Antibody specificity is described in greater detail below. However, it should be emphasized that antibodies that can be generated from polypeptides that have previously been described in the literature and that are capable of fortuitously cross-reacting with nGPCR-x (*e.g.*, due to the fortuitous existence of a similar epitope in both polypeptides) are considered "cross-reactive" antibodies. Such cross-reactive antibodies are not antibodies that are "specific" for nGPCR-x. The determination of whether an antibody is specific for nGPCR-x or is cross-reactive with another known receptor is made using any of several assays, such as Western blotting assays, that are well known in the art. For identifying cells that express nGPCR-x and also for modulating nGPCR-x-ligand binding activity, antibodies that specifically bind to an extracellular epitope of the nGPCR-x are preferred.

[000128] In one preferred variation, the invention provides monoclonal antibodies. Hybridomas that produce such antibodies also are intended as aspects of the invention. In yet another variation, the invention provides a humanized antibody. Humanized antibodies are useful for *in vivo* therapeutic indications.

[000129] In another variation, the invention provides a cell-free composition comprising polyclonal antibodies, wherein at least one of the antibodies is an antibody of the invention specific for nGPCR-x. Antisera isolated from an animal is an exemplary composition, as is a composition comprising an antibody fraction of an antisera that has been resuspended in water or in another diluent, excipient, or carrier.

[000130] In still another related embodiment, the invention provides an anti-idiotypic antibody specific for an antibody that is specific for nGPCR-x.

[000131] It is well known that antibodies contain relatively small antigen binding domains that can be isolated chemically or by recombinant techniques. Such domains are useful nGPCR-x binding molecules themselves, and also may be reintroduced into human antibodies, or fused to toxins or other polypeptides. Thus, in still another embodiment, the invention provides a polypeptide comprising a fragment of a nGPCR-x-specific antibody, wherein the fragment and the polypeptide bind to the nGPCR-x. By way of non-limiting example, the invention provides polypeptides that are single chain antibodies and CDR-grafted antibodies.

[000132] Non-human antibodies may be humanized by any of the methods known in the art. In one method, the non-human CDRs are inserted into a human antibody or consensus antibody framework sequence. Further changes can then be introduced into the antibody framework to modulate affinity or immunogenicity.

[000133] Antibodies of the invention are useful for, *e.g.*, therapeutic purposes (by modulating activity of nGPCR-x), diagnostic purposes to detect or quantitate nGPCR-x, and purification of nGPCR-x. Kits comprising an antibody of the invention for any of the purposes described herein are also comprehended. In general, a kit of the invention also includes a control antigen for which the antibody is immunospecific.

Compositions

[000134] Mutations in the nGPCR-x gene that result in loss of normal function of the nGPCR-x gene product underlie nGPCR-x-related human disease states. The invention comprehends gene therapy to restore nGPCR-x activity to treat those disease states. Delivery of a functional nGPCR-x gene to appropriate cells is effected *ex vivo*, *in situ*, or *in vivo* by use of vectors, and more particularly viral vectors (*e.g.*, adenovirus, adeno-associated virus, or a retrovirus), or *ex vivo* by use of physical DNA transfer methods (*e.g.*, liposomes or chemical treatments). See, for example, Anderson, *Nature*, supplement to vol. 392, no. 6679, pp.25-20 (1998). For additional reviews of gene therapy technology see Friedmann, *Science, 244*: 1275-1281 (1989); Verma, *Scientific American*: 68-84 (1990); and Miller, *Nature, 357*: 455-460 (1992). Alternatively, it is contemplated that in other human disease states, preventing the expression of, or inhibiting the activity of, nGPCR-x will be useful in treating disease states. It is contemplated that antisense therapy or gene therapy could be applied to negatively regulate the expression of nGPCR-x.

[000135] Another aspect of the present invention is directed to compositions, including pharmaceutical compositions, comprising any of the nucleic acid molecules or recombinant expression vectors described above and an acceptable carrier or diluent. Preferably, the carrier or diluent is pharmaceutically acceptable. Suitable carriers are described in the most recent

edition of *Remington's Pharmaceutical Sciences*, A. Osol, a standard reference text in this field, which is incorporated herein by reference in its entirety. Preferred examples of such carriers or diluents include, but are not limited to, water, saline, Ringer's solution, dextrose solution, and 5% human serum albumin. Liposomes and nonaqueous vehicles such as fixed oils may also be used. The formulations are sterilized by commonly used techniques.

[000136] Also within the scope of the invention are compositions comprising polypeptides, polynucleotides, or antibodies of the invention that have been formulated with, *e.g.*, a pharmaceutically acceptable carrier.

[000137] The invention also provides methods of using antibodies of the invention. For example, the invention provides a method for modulating ligand binding of a nGPCR-x comprising the step of contacting the nGPCR-x with an antibody specific for the nGPCR-x, under conditions wherein the antibody binds the receptor.

[000138] As discussed above, it is well known that GPCRs are expressed in many different tissues and regions, including in the brain. GPCRs that may be expressed in the brain, such as nGPCR-x, provide an indication that aberrant nGPCR-x signaling activity may correlate with one or more neurological or psychological disorders. The invention also provides a method for treating a neurological or psychiatric disorder comprising the step of administering to a mammal in need of such treatment an amount of an antibody-like polypeptide of the invention that is sufficient to modulate ligand binding to a nGPCR-x in neurons of the mammal. nGPCR-x may also be expressed in other tissues, including but not limited to, peripheral blood lymphocytes, pancreas, ovary, uterus, testis, salivary gland, thyroid gland, kidney, adrenal gland, liver, bone marrow, prostate, fetal liver, colon, muscle, and fetal brain, and may be found in many other tissues. Within the brain, nGPCR-x mRNA transcripts may be found in many tissues, including, but not limited to, frontal lobe, hypothalamus, pons, cerebellum, caudate nucleus, and medulla.

Kits

[000139] The present invention is also directed to kits, including pharmaceutical kits. The kits can comprise any of the nucleic acid molecules described above, any of the polypeptides described above, or any antibody which binds to a polypeptide of the invention as described above, as well as a negative control. The kit preferably comprises additional components, such as, for example, instructions, solid support, reagents helpful for quantification, and the like.

[000140] In another aspect, the invention features methods for detection of a polypeptide in a sample as a diagnostic tool for diseases or disorders, wherein the method comprises the steps of: (a) contacting the sample with a nucleic acid probe which hybridizes under hybridization assay conditions to a nucleic acid target region of a polypeptide having sequences selected from the group consisting of SEQ ID NO:129 to SEQ ID NO:257, said probe comprising the nucleic acid

sequence encoding the polypeptide, fragments thereof, and the complements of the sequences and fragments; and (b) detecting the presence or amount of the probe:target region hybrid as an indication of the disease.

[000141] In preferred embodiments of the invention, the disease is selected from the group consisting of thyroid disorders (*e.g.* thyreotoxicosis, myxoedema); renal failure; inflammatory conditions (*e.g.*, Crohn's disease); diseases related to cell differentiation and homeostasis; rheumatoid arthritis; autoimmune disorders; movement disorders; CNS disorders (*e.g.*, pain including migraine; stroke; psychotic and neurological disorders, including anxiety, mental disorder, manic depression, anxiety, generalized anxiety disorder, post-traumatic-stress disorder, depression, bipolar disorder, delirium, dementia, severe mental retardation; dyskinesias, such as Huntington's disease or Tourette's Syndrome; attention disorders including ADD and ADHD, and degenerative disorders such as Parkinson's, Alzheimer's; movement disorders, including ataxias, supranuclear palsy, *etc.*); infections, such as viral infections caused by HIV-1 or HIV-2; metabolic and cardiovascular diseases and disorders (*e.g.*, type 2 diabetes, impaired glucose tolerance, dyslipidemia, obesity, anorexia, hypotension, hypertension, thrombosis, myocardial infarction, cardiomyopathies, atherosclerosis, *etc.*); proliferative diseases and cancers (*e.g.*, different cancers such as breast, colon, lung, *etc.*, and hyperproliferative disorders such as psoriasis, prostate hyperplasia, *etc.*); hormonal disorders (*e.g.*, male/female hormonal replacement, polycystic ovarian syndrome, alopecia, *etc.*); and sexual dysfunction, among others.

[000142] Kits may be designed to detect either expression of polynucleotides encoding nGPCR-x expressed in the brain or the nGPCR-x proteins themselves in order to identify tissue as being neurological. For example, oligonucleotide hybridization kits can be provided which include a container having an oligonucleotide probe specific for the nGPCR-x-specific DNA and optionally, containers with positive and negative controls and/or instructions. Similarly, PCR kits can be provided which include a container having primers specific for the nGPCR-x-specific sequences, DNA and optionally, containers with size markers, positive and negative controls and/or instructions.

[000143] Hybridization conditions should be such that hybridization occurs only with the genes in the presence of other nucleic acid molecules. Under stringent hybridization conditions only highly complementary nucleic acid sequences hybridize. Preferably, such conditions prevent hybridization of nucleic acids having 1 or 2 mismatches out of 20 contiguous nucleotides. Such conditions are defined supra.

[000144] The diseases for which detection of genes in a sample could be diagnostic include diseases in which nucleic acid (DNA and/or RNA) is amplified in comparison to normal cells.

By "amplification" is meant increased numbers of DNA or RNA in a cell compared with normal cells.

[000145] The diseases that could be diagnosed by detection of nucleic acid in a sample preferably include central nervous system and metabolic diseases. The test samples suitable for nucleic acid probing methods of the present invention include, for example, cells or nucleic acid extracts of cells, or biological fluids. The samples used in the above-described methods will vary based on the assay format, the detection method and the nature of the tissues, cells or extracts to be assayed. Methods for preparing nucleic acid extracts of cells are well known in the art and can be readily adapted in order to obtain a sample that is compatible with the method utilized.

[000146] Alternatively, immunoassay kits can be provided which have containers container having antibodies specific for the nGPCR-x-protein and optionally, containers with positive and negative controls and/or instructions.

[000147] Kits may also be provided useful in the identification of GPCR binding partners such as natural ligands or modulators (agonists or antagonists). Substances useful for treatment of disorders or diseases preferably show positive results in one or more *in vitro* assays for an activity corresponding to treatment of the disease or disorder in question. Substances that modulate the activity of the polypeptides preferably include, but are not limited to, antisense oligonucleotides, agonists and antagonists, and inhibitors of protein kinases.

Methods of inducing immune response

[000148] Another aspect of the present invention is directed to methods of inducing an immune response in a mammal against a polypeptide of the invention by administering to the mammal an amount of the polypeptide sufficient to induce an immune response. The amount willbe dependent on the animal species, size of the animal, and the like but can be determined by those skilled in the art.

Methods of identifying ligands

[000149] The invention also provides assays to identify compounds that bind nGPCR-x. One such assay comprises the steps of: (a) contacting a composition comprising a nGPCR-x with a compound suspected of binding nGPCR-x; and (b) measuring binding between the compound and nGPCR-x. In one variation, the composition comprises a cell expressing nGPCR-x on its surface. In another variation, isolated nGPCR-x or cell membranes comprising nGPCR-x are employed. The binding may be measured directly, *e.g.*, by using a labeled compound, or may be measured indirectly by several techniques, including measuring intracellular signaling of nGPCR-x induced by the compound (or measuring changes in the level of nGPCR-x signaling). Following steps (a) and (b), compounds identified as binding nGPCR-x may be tested in other

assays including, but not limited to, *in vivo* models, to confirm or quantitate binding to nGPCR-x.

[000150] Specific binding molecules, including natural ligands and synthetic compounds, can be identified or developed using isolated or recombinant nGPCR-x products, nGPCR-x variants, or preferably, cells expressing such products. Binding partners are useful for purifying nGPCR-x products and detection or quantification of nGPCR-x products in fluid and tissue samples using known immunological procedures. Binding molecules are also manifestly useful in modulating (*i.e.*, blocking, inhibiting or stimulating) biological activities of nGPCR-x, especially those activities involved in signal transduction.

[000151] The DNA and amino acid sequence information provided by the present invention also makes possible identification of binding partner compounds with which a nGPCR-x polypeptide or polynucleotide will interact. Methods to identify binding partner compounds include solution assays, *in vitro* assays wherein nGPCR-x polypeptides are immobilized, and cell-based assays. Identification of binding partner compounds of nGPCR-x polypeptides provides candidates for therapeutic or prophylactic intervention in pathologies associated with nGPCR-x normal and aberrant biological activity.

[000152] The invention includes several assay systems for identifying nGPCR-x binding partners. In solution assays, methods of the invention comprise the steps of (a) contacting a nGPCR-x polypeptide with one or more candidate binding partner compounds and (b) identifying the compounds that bind to the nGPCR-x polypeptide. Identification of the compounds that bind the nGPCR-x polypeptide can be achieved by isolating the nGPCR-x polypeptide/binding partner complex, and separating the binding partner compound from the nGPCR-x polypeptide. An additional step of characterizing the physical, biological, and/or biochemical properties of the binding partner compound is also comprehended in another embodiment of the invention, wherein compounds identified as binding nGPCR-x may be tested in other assays including, but not limited to, *in vivo* models, to confirm or quantitate binding to nGPCR-x. In one aspect, the nGPCR-x polypeptide/binding partner complex is isolated using an antibody immunospecific for either the nGPCR-x polypeptide or the candidate binding partner compound.

[000153] In still other embodiments, either the nGPCR-x polypeptide or the candidate binding partner compound comprises a label or tag that facilitates its isolation, and methods of the invention to identify binding partner compounds include a step of isolating the nGPCR-x polypeptide/binding partner complex through interaction with the label or tag. An exemplary tag of this type is a poly-histidine sequence, generally around six histidine residues, that permits isolation of a compound so labeled using nickel chelation. Other labels and tags, such as the

FLAG® tag (Eastman Kodak, Rochester, NY), well known and routinely used in the art, are embraced by the invention.

[000154] In one variation of an *in vitro* assay, the invention provides a method comprising the steps of (a) contacting an immobilized nGPCR-x polypeptide with a candidate binding partner compound and (b) detecting binding of the candidate compound to the nGPCR-x polypeptide. In an alternative embodiment, the candidate binding partner compound is immobilized and binding of nGPCR-x is detected. Immobilization is accomplished using any of the methods well known in the art, including covalent bonding to a support, a bead, or a chromatographic resin, as well as non-covalent, high affinity interactions such as antibody binding, or use of streptavidin/biotin binding wherein the immobilized compound includes a biotin moiety. Detection of binding can be accomplished (i) using a radioactive label on the compound that is not immobilized, (ii) using of a fluorescent label on the non-immobilized compound, (iii) using an antibody immunospecific for the non-immobilized compound, (iv) using a label on the non-immobilized compound that excites a fluorescent support to which the immobilized compound is attached, as well as other techniques well known and routinely practiced in the art.

[000155] The invention also provides cell-based assays to identify binding partner compounds of a nGPCR-x polypeptide. In one embodiment, the invention provides a method comprising the steps of contacting a nGPCR-x polypeptide expressed on the surface of a cell with a candidate binding partner compound and detecting binding of the candidate binding partner compound to the nGPCR-x polypeptide. In a preferred embodiment, the detection comprises detecting a calcium flux or other physiological event in the cell caused by the binding of the molecule.

[000156] Another aspect of the present invention is directed to methods of identifying compounds that bind to either nGPCR-x or nucleic acid molecules encoding nGPCR-x, comprising contacting nGPCR-x, or a nucleic acid molecule encoding the same, with a compound, and determining whether the compound binds nGPCR-x or a nucleic acid molecule encoding the same. Binding can be determined by binding assays which are well known to the skiled artisan, including, but not limited to, gel-shift assays, Western blots, radiolabeled competition assay, phage-based expression cloning, co-fractionation by chromatography, co-precipitation, cross linking, interaction trap/two-hybrid analysis, southwestern analysis, ELISA, and the like, which are described in, for example, *Current Protocols in Molecular Biology*, **1999**, John Wiley & Sons, NY, which is incorporated herein by reference in its entirety. The compounds to be screened include (which may include compounds which are suspected to bind nGPCR-x, or a nucleic acid molecule encoding the same), but are not limited to, extracellular, intracellular, biologic or chemical origin. The methods of the invention also embrace ligands, especially neuropeptides, that are attached to a label, such as a radiolabel (*e.g.*, ^{125}I,^{35}S, ^{32}P, ^{33}P, ^{3}H), a

fluorescence label, a chemiluminescent label, an enzymic label and an immunogenic label. Modulators falling within the scope of the invention include, but are not limited to, non-peptide molecules such as non-peptide mimetics, non-peptide allosteric effectors, and peptides. The nGPCR-x polypeptide or polynucleotide employed in such a test may either be free in solution, attached to a solid support, borne on a cell surface or located intracellularly or associated with a portion of a cell. One skilled in the art can, for example, measure the formation of complexes between nGPCR-x and the compound being tested. Alternatively, one skilled in the art can examine the diminution in complex formation between nGPCR-x and its substrate caused by the compound being tested.

[000157] In another embodiment of the invention, high throughput screening for compounds having suitable binding affinity to nGPCR-x is employed. Briefly, large numbers of different test compounds are synthesized on a solid substrate. The peptide test compounds are contacted with nGPCR-x and washed. Bound nGPCR-x is then detected by methods well known in the art. Purified polypeptides of the invention can also be coated directly onto plates for use in the aforementioned drug screening techniques. In addition, non-neutralizing antibodies can be used to capture the protein and immobilize it on the solid support.

[000158] Generally, an expressed nGPCR-x can be used for HTS binding assays in conjunction with its defined ligand, in this case the corresponding neuropeptide that activates it. The identified peptide is labeled with a suitable radioisotope, including, but not limited to, ^{125}I, ^{3}H, ^{35}S or ^{32}P, by methods that are well known to those skilled in the art. Alternatively, the peptides may be labeled by well-known methods with a suitable fluorescent derivative (Baindur *et al.*, *Drug Dev. Res.*, **1994**, *33*, 373-398; Rogers, *Drug Discovery Today*, **1997**, *2*, 156-160). Radioactive ligand specifically bound to the receptor in membrane preparations made from the cell line expressing the recombinant protein can be detected in HTS assays in one of several standard ways, including filtration of the receptor-ligand complex to separate bound ligand from unbound ligand (Williams, *Med. Res. Rev.*, **1991**, *11*, 147-184; Sweetnam *et al.*, *J. Natural Products*, **1993**, *56*, 441-455). Alternative methods include a scintillation proximity assay (SPA) or a FlashPlate format in which such separation is unnecessary (Nakayama, *Cur. Opinion Drug Disc. Dev.*, **1998**, *1*, 85-91 Bossé *et al.*, *J. Biomolecular Screening*, **1998**, *3*, 285-292.). Binding of fluorescent ligands can be detected in various ways, including fluorescence energy transfer (FRET), direct spectrophotofluorometric analysis of bound ligand, or fluorescence polarization (Rogers, *Drug Discovery Today*, **1997**, *2*, 156-160; Hill, *Cur. Opinion* Drug Disc. *Dev.*, **1998**, *1*, 92-97).

[000159] Other assays may be used to identify specific ligands of a nGPCR-x receptor, including assays that identify ligands of the target protein through measuring direct binding of test ligands

to the target protein, as well as assays that identify ligands of target proteins through affinity ultrafiltration with ion spray mass spectroscopy/HPLC methods or other physical and analytical methods. Alternatively, such binding interactions are evaluated indirectly using the yeast two-hybrid system described in Fields *et al.*, Nature, 340:245-246 (1989), and Fields*et al.*, Trends in Genetics, 10:286-292 (1994), both of which are incorporated herein by reference. The two-hybrid system is a genetic assay for detecting interactions between two proteins or polypeptides. It can be used to identify proteins that bind to a known protein of interest, or to delineate domains or residues critical for an interaction. Variations on this methodology have been developed to clone genes that encode DNA binding proteins, to identify peptides that bind to a protein, and to screen for drugs. The two-hybrid system exploits the ability of a pair of interacting proteins to bring a transcription activation domain into close proximity with a DNA binding domain that binds to an upstream activation sequence (UAS) of a reporter gene, and is generally performed in yeast. The assay requires the construction of two hybrid genes encoding (1) a DNA-binding domain that is fused to a first protein and (2) an activation domain fused to a second protein. The DNA-binding domain targets the first hybrid protein to the UAS of the reporter gene; however, because most proteins lack an activation domain, this DNA-binding hybrid protein does not activate transcription of the reporter gene. The second hybrid protein, which contains the activation domain, cannot by itself activate expression of the reporter gene because it does not bind the UAS. However, when both hybrid proteins are present, the noncovalent interaction of the first and second proteins tethers the activation domain to the UAS, activating transcription of the reporter gene. For example, when the first protein is a GPCR gene product, or fragment thereof, that is known to interact with another protein or nucleic acid, this assay can be used to detect agents that interfere with the binding interaction. Expression of the reporter gene is monitored as different test agents are added to the system. The presence of an inhibitory agent results in lack of a reporter signal.

[000160] The yeast two-hybrid assay can also be used to identify proteins that bind to the gene product. In an assay to identify proteins that bind to a nGPCR-x receptor, or fragment thereof, a fusion polynucleotide encoding both a nGPCR-x receptor (or fragment) and a UAS binding domain (*i.e.*, a first protein) may be used. In addition, a large number of hybrid genes each encoding a different second protein fused to an activation domain are produced and screened in the assay. Typically, the second protein is encoded by one or more members of a total cDNA or genomic DNA fusion library, with each second protein-coding region being fused to the activation domain. This system is applicable to a wide variety of proteins, and it is not even necessary to know the identity or function of the second binding protein. The system is highly sensitive and can detect interactions not revealed by other methods; even transient interactions

may trigger transcription to produce a stable mRNA that can be repeatedly translated to yield the reporter protein.

[000161] Other assays may be used to search for agents that bind to the target protein. One such screening method to identify direct binding of test ligands to a target protein is described in U.S. Patent No. 5,585,277, incorporated herein by reference. This method relies on the principle that proteins generally exist as a mixture of folded and unfolded states, and continually alternate between the two states. When a test ligand binds to the folded form of a target protein (*i.e*, when the test ligand is a ligand of the target protein), the target protein molecule bound by the ligand remains in its folded state. Thus, the folded target protein is present to a greater extent in the presence of a test ligand which binds the target protein, than in the absence of a ligand. Binding of the ligand to the target protein can be determined by any method that distinguishes between the folded and unfolded states of the target protein. The function of the target protein need not be known in order for this assay to be performed. Virtually any agent can be assessed by this method as a test ligand, including, but not limited to, metals, polypeptides, proteins, lipids, polysaccharides, polynucleotides and small organic molecules.

[000162] Another method for identifying ligands of a target protein is described in Wieboldt *et al.*, Anal. Chem., 69:1683-1691 (1997), incorporated herein by reference. This technique screens combinatorial libraries of 20-30 agents at a time in solution phase for binding to the target protein. Agents that bind to the target protein are separated from other library components by simple membrane washing. The specifically selected molecules that are retained on the filter are subsequently liberated from the target protein and analyzed by HPLC and pneumatically assisted electrospray (ion spray) ionization mass spectroscopy. This procedure selects library components with the greatest affinity for the target protein, and is particularly useful for small molecule libraries.

[000163] Other embodiments of the invention comprise using competitive screening assays in which neutralizing antibodies capable of binding a polypeptide of the invention specifically compete with a test compound for binding to the polypeptide. In this manner, the antibodies can be used to detect the presence of any peptide that shares one or more antigenic determinants with nGPCR-x. Radiolabeled competitive binding studies are described in A.H. Lin *et al.* *Antimicrobial Agents and Chemotherapy*, **1997**, vol. 41, no. 10. pp. 2127-2131, the disclosure of which is incorporated herein by reference in its entirety.

Identification of modulating agents

[000164] The invention also provides methods for identifying a modulator of binding between a nGPCR-x and a nGPCR-x binding partner, comprising the steps of: (a) contacting a nGPCR-x binding partner and a composition comprising a nGPCR-x in the presence and in the absence of

a putative modulator compound; (b) detecting binding between the binding partner and the nGPCR-x; and (c) identifying a putative modulator compound or a modulator compound in view of decreased or increased binding between the binding partner and the nGPCR-x in the presence of the putative modulator, as compared to binding in the absence of the putative modulator. Following steps (a) and (b), compounds identified as modulating binding between nGPCR-x and a nGPCR-x binding partner may be tested in other assays including, but not limited to, *in vivo* models, to confirm or quantitate modulation of binding to nGPCR-x.

[000165] nGPCR-x binding partners that stimulate nGPCR-x activity are useful as agonists in disease states or conditions characterized by insufficient nGPCR-x signaling (*e.g.*, as a result of insufficient activity of a nGPCR-x ligand). nGPCR-x binding partners that block ligand-mediated nGPCR-x signaling are useful as nGPCR-x antagonists to treat disease states or conditions characterized by excessive nGPCR-x signaling. In addition nGPCR-x modulators in general, as well as nGPCR-x polynucleotides and polypeptides, are useful in diagnostic assays for such diseases or conditions.

[000166] In another aspect, the invention provides methods for treating a disease or abnormal condition by administering to a patient in need of such treatment a substance that modulates the activity or expression of a polypeptide having sequences selected from the group consisting of SEQ ID NO:129 to SEQ ID NO:257.

[000167] Agents that modulate (*i.e.*, increase, decrease, or block) nGPCR-x activity or expression may be identified by incubating a putative modulator with a cell containing a nGPCR-x polypeptide or polynucleotide and determining the effect of the putative modulator on nGPCR-x activity or expression. The selectivity of a compound that modulates the activity of nGPCR-x can be evaluated by comparing its effects on nGPCR-x to its effect on other GPCR compounds. Following identification of compounds that modulate nGPCR-x activity or expression, such compounds may be further tested in other assays including, but not limited to, *in vivo* models, in order to confirm or quantitate their activity. Selective modulators may include, for example, antibodies and other proteins, peptides, or organic molecules that specifically bind to a nGPCR-x polypeptide or a nGPCR-x-encoding nucleic acid. Modulators of nGPCR-x activity will be therapeutically useful in treatment of diseases and physiological conditions in which normal or aberrant nGPCR-x activity is involved. nGPCR-x polynucleotides, polypeptides, and modulators may be used in the treatment of such diseases and conditions as infections, such as viral infections caused by HIV-1 or HIV-2; pain; cancers; metabolic and cardiovascular diseases and disorders (*e.g.*, type 2 diabetes, impaired glucose tolerance, dyslipidemia, obesity, anorexia, hypotension, hypertension, thrombosis, myocardial infarction, cardiomyopathies, atherosclerosis, *etc.*); Parkinson's disease; and psychotic and neurological disorders, including

schizophrenia, migraine, ADHH, major depression, anxiety, mental disorder, manic depression, delirium, dementia, severe mental retardation and dyskinesias, such as Huntington's disease or Tourette's Syndrome, among others. nGPCR-x polynucleotides and polypeptides, as well as nGPCR-x modulators, may also be used in diagnostic assays for such diseases or conditions.

[000168] Methods of the invention to identify modulators include variations on any of the methods described above to identify binding partner compounds, the variations including techniques wherein a binding partner compound has been identified and the binding assay is carried out in the presence and absence of a candidate modulator. A modulator is identified in those instances where binding between the nGPCR-x polypeptide and the binding partner compound changes in the presence of the candidate modulator compared to binding in the absence of the candidate modulator compound. A modulator that increases binding between the nGPCR-x polypeptide and the binding partner compound is described as an enhancer or activator, and a modulator that decreases binding between the nGPCR-x polypeptide and the binding partner compound is described as an inhibitor. Following identification of modulators, such compounds may be further tested in other assays including, but not limited to, *in vivo* models, in order to confirm or quantitate their activity as modulators.

[000169] The invention also comprehends high-throughput screening (HTS) assays to identify compounds that interact with or inhibit biological activity (*i.e.*, affect enzymatic activity, binding activity, *etc.*) of a nGPCR-x polypeptide. HTS assays permit screening of large numbers of compounds in an efficient manner. Cell-based HTS systems are contemplated to investigate nGPCR-x receptor-ligand interaction. HTS assays are designed to identify "hits" or "lead compounds" having the desired property, from which modifications can be designed to improve the desired property. Chemical modification of the "hit" or "lead compound" is often based on an identifiable structure/activity relationship between the "hit" and the nGPCR-x polypeptide.

[000170] Another aspect of the present invention is directed to methods of identifying compounds which modulate (*i.e.*, increase or decrease) an activity of nGPCR-x comprising contacting nGPCR-x with a compound, and determining whether the compound modifies activity of nGPCR-x. The activity in the presence of the test compared is measured to the activity in the absence of the test compound. Where the activity of the sample containing the test compound is higher than the activity in the sample lacking the test compound, the compound will have increased activity. Similarly, where the activity of the sample containing the test compound is lower than the activity in the sample lacking the test compound, the compound will have inhibited activity. Following the identification of compounds that modulate an activity of

nGPCR-x, such compounds can be further tested in other assays including, but notlimited to, *in vivo* models, in order to confirm or quantitate their activity.

[000171] The present invention is particularly useful for screening compounds by using nGPCR-x in any of a variety of drug screening techniques. The compounds to be screened include (which may include compounds which are suspected to modulate nGPCR-x activity), but are not limited to, extracellular, intracellular, biologic or chemical origin. The nGPCR-x polypeptide employed in such a test may be in any form, preferably, free in solution, attached to a solid support, borne on a cell surface or located intracellularly. One skilled in the art can, for example, measure the formation of complexes between nGPCR-x and the compound being tested. Alternatively, one skilled in the art can examine the diminution in complex formation between nGPCR-x and its substrate caused by the compound being tested.

[000172] The activity of nGPCR-x polypeptides of the invention can be determined by, for example, examining the ability to bind or be activated by chemically synthesized peptide ligands. Alternatively, the activity of nGPCR-x polypeptides can be assayed by examining their ability to bind calcium ions, hormones, chemokines, neuropeptides, neurotransmitters, nucleotides, lipids, odorants, and photons. Alternatively, the activity of the nGPCR-x polypeptides can be determined by examining the activity of effector molecules including, but not limited to, adenylate cyclase, phospholipases and ion channels. Thus, modulators of nGPCR-x polypeptide activity may alter a GPCR receptor function, such as a binding property of a receptor or an activity such as G protein-mediated signal transduction or membrane localization. In various embodiments of the method, the assay may take the form of an ion flux assay, a yeast growth assay, a non-hydrolyzable GTP assay such as a [^{35}S]-GTP γS assay, a cAMP assay, an inositol triphosphate assay, a diacylglycerol assay, an Aequorin assay, a Luciferase assay, a FLIPR assay for intracellular Ca^{2+} concentration, a mitogenesis assay, a MAP Kinase activity assay, an arachidonic acid release assay (*e.g.*, using [^{3}H]-arachidonic acid), and an assay for extracellular acidification rates, as well as other binding or function-based assays of nGPCR-x activity that are generally known in the art. In several of these embodiments, the invention comprehends the inclusion of any of the G proteins known in the art, such as G_{16}, G_{15}, or chimeric G_{qd5} , G_{qs5}, G_{qo5}, G_{q25}, and the like. nGPCRx activity can be determined by methodologies that are used to assay for FaRP activity, which is well known to those skilled in the art. Biological activities of nGPCR-x receptors according to the invention include, but are not limited to, the binding of a natural or an unnatural ligand, as well as any one of the functional activities of GPCRs known in the art. Non-limiting examples of GPCR activities include transmembrane signaling of various forms, which may involve G protein association and/or the exertion of an influence over G protein binding of various guanidylate

nucleotides; another exemplary activity of GPCRs is the binding of accessory proteins or polypeptides that differ from known G proteins.

[000173] The modulators of the invention exhibit a variety of chemical structures, which can be generally grouped into non-peptide mimetics of natural GPCR receptor ligands, peptide and non-peptide allosteric effectors of GPCR receptors, and peptides that may function as activators or inhibitors (competitive, uncompetitive and non-competitive) (*e.g.*, antibody products) of GPCR receptors. The invention does not restrict the sources for suitable modulators, which may be obtained from natural sources such as plant, animal or mineral extracts, or non-natural sources such as small molecule libraries, including the products of combinatorial chemical approaches to library construction, and peptide libraries. Examples of peptide modulators of GPCR receptors exhibit the following primary structures: GLGPRPLRFamide, GNSFLRFamide, GGPQGPLRFamide, GPSGPLRFamide, PDVDHVFLRFamide, and pyro-EDVDHVFLRFamide.

[000174] Other assays can be used to examine enzymatic activity including, but not limited to, photometric, radiometric, HPLC, electrochemical, and the like, which are described in, for example, *Enzyme Assays: A Practical Approach*, eds. R. Eisenthal and M. J. Danson, **1992**, Oxford University Press, which is incorporated herein by reference in its entirety.

[000175] The use of cDNAs encoding GPCRs in drug discovery programs is well-known; assays capable of testing thousands of unknown compounds per day in high-throughput screens (HTSs) are thoroughly documented. The literature is replete with examples of the use of radiolabeled ligands in HTS binding assays for drug discovery (see Williams, *Medicinal Research Reviews*, **1991**, *11*, 147-184.; Sweetnam, *et al.*, *J. Natural Products*, **1993**, *56*, 441-455 for review). Recombinant receptors are preferred for binding assay HTS because they allow for better specificity (higher relative purity), provide the ability to generate large amounts of receptor material, and can be used in a broad variety of formats (see Hodgson, *Bio/Technology*, **1992**, *10*, 973-980; each of which is incorporated herein by reference in its entirety).

[000176] A variety of heterologous systems is available for functional expression of recombinant receptors that are well known to those skilled in the art. Such systems include bacteria (Strosberg, *et al.*, *Trends in Pharmacological Sciences*, **1992**, *13*, 95-98), yeast (Pausch, *Trends in Biotechnology*, **1997**, *15*, 487-494), several kinds of insect cells (Vanden Broeck, *Int. Rev. Cytology*, **1996**, *164*, 189-268), amphibian cells (Jayawickreme *et al.*, *Current Opinion in Biotechnology*, **1997**, *8*, 629-634) and several mammalian cell lines (CHO, HEK-293, COS, etc.; see Gerhardt, *et al.*, *Eur. J. Pharmacology*, **1997**, *334*, 1-23). These examples do not preclude the use of other possible cell expression systems, including cell lines obtained from nematodes (PCT application WO 98/37177).

[000177] In preferred embodiments of the invention, methods of screening for compounds that modulate nGPCR-x activity comprise contacting test compounds with nGPCR-x and assaying for the presence of a complex between the compound and nGPCR-x. In such assays, the ligand is typically labeled. After suitable incubation, free ligand is separated from that present in bound form, and the amount of free or uncomplexed label is a measure of the ability of the particular compound to bind to nGPCR-x.

[000178] It is well known that activation of heterologous receptors expressed in recombinant systems results in a variety of biological responses, which are mediated by G proteins expressed in the host cells. Occupation of a GPCR by an agonist results in exchange of bound GDP for GTP at a binding site on the G_α subunit; one can use a radioactive, non-hydrolyzable derivative of GTP, GTPγ[^{35}S], to measure binding of an agonist to the receptor (Sim *et al.*, Neuroreport, **1996**, *7*, 729-733). One can also use this binding to measure the ability of antagonists to bind to the receptor by decreasing binding of GTPγ[^{35}S] in the presence of a known agonist. One could therefore construct a HTS based on GTPγ[^{35}S] binding, though this is not the preferred method.

[000179] The G proteins required for functional expression of heterologous GPCRs can be native constituents of the host cell or can be introduced through well-known recombinant technology. The G proteins can be intact or chimeric. Often, a nearly universally competent G protein (e.g., $G_{\alpha 16}$) is used to couple any given receptor to a detectable response pathway. G protein activation results in the stimulation or inhibition of other native proteins, events that can be linked to a measurable response.

[000180] Examples of such biological responses include, but are not limited to, the following: the ability to survive in the absence of a limiting nutrient in specifically engineered yeast cells (Pausch, *Trends in Biotechnology*, **1997**, *15*, 487-494); changes in intracellular Ca^{2+} concentration as measured by fluorescent dyes (Murphy, *et al.*, *Cur. Opinion Drug Disc. Dev.*, **1998**, *1*, 192-199). Fluorescence changes can also be used to monitor ligand-induced changes in membrane potential or intracellular pH; an automated system suitable for HTS has been described for these purposes (Schroeder, *et al.*, *J. Biomolecular Screening*, **1996**, *1*, 75-80). Melanophores prepared from *Xenopus laevis* show a ligand-dependent change in pigment organization in response to heterologous GPCR activation; this response is adaptable to HTS formats (Jayawickreme *et al.*, *Cur. Opinion Biotechnology*, **1997**, *8*, 629-634). Assays are also available for the measurement of common second messengers, including cAMP, phosphoinositides and arachidonic acid, but these are not generally preferred for HTS.

[000181] Preferred methods of HTS employing these receptors include permanently transfected CHO cells, in which agonists and antagonists can be identified by the ability to specifically alter the binding of GTPγ[^{35}S] in membranes prepared from these cells. In another embodiment of

the invention, permanently transfected CHO cells could be used for the preparation of membranes which contain significant amounts of the recombinant receptor proteins; these membrane preparations would then be used in receptor binding assays, employing the radiolabeled ligand specific for the particular receptor. Alternatively, a functional assay, such as fluorescent monitoring of ligand-induced changes in internal Ca^{2+} concentration or membrane potential in permanently transfected CHO cells containing each of these receptors individually or in combination would be preferred for HTS. Equally preferred would be an alternative type of mammalian cell, such as HEK-293 or COS cells, in similar formats. More preferred would be permanently transfected insect cell lines, such as *Drosophila* S2 cells. Even more preferred would be recombinant yeast cells expressing the *Drosophila melanogaster* receptors in HTS formats well known to those skilled in the art (*e.g.*, Pausch, *Trends in Biotechnology*, **1997**, *15*, 487-494).

[000182] The invention contemplates a multitude of assays to screen and identify inhibitors of ligand binding to nGPCR-x receptors. In one example, the nGPCR-x receptor is immobilized and interaction with a binding partner is assessed in the presence and absence of a candidate modulator such as an inhibitor compound. In another example, interaction between the nGPCR-x receptor and its binding partner is assessed in a solution assay, both in the presence and absence of a candidate inhibitor compound. In either assay, an inhibitor is identified as a compound that decreases binding between the nGPCR-x receptor and its binding partner. Following the identification of compounds which inhibit ligand binding to nGPCR-x receptors, such compounds may be further tested in other assays including, but not limited to, *in vivo* models, in order to confirm or quantitate their activity. Another contemplated assay involves a variation of the dihybrid assay wherein an inhibitor of protein/protein interactions is identified by detection of a positive signal in a transformed or transfected host cell, as described in PCT publication number WO 95/20652, published August 3, 1995.

[000183] Candidate modulators contemplated by the invention include compounds selected from libraries of either potential activators or potential inhibitors. There are a number of different libraries used for the identification of small molecule modulators, including: (1) chemical libraries, (2) natural product libraries, and (3) combinatorial libraries comprised of random peptides, oligonucleotides or organic molecules. Chemical libraries consist of random chemical structures, some of which are analogs of known compounds or analogs of compounds that have been identified as "hits" or "leads" in other drug discovery screens, some of which are derived from natural products, and some of which arise from non-directed synthetic organic chemistry. Natural product libraries are collections of microorganisms, animals, plants, or marine organisms which are used to create mixtures for screening by: (1) fermentation and extraction

of broths from soil, plant or marine microorganisms or (2) extraction of plants or marine organisms. Natural product libraries include polyketides, non-ribosomal peptides, and variants (non-naturally occurring) thereof. For a review, see Science 282:63-68 (1998). Combinatorial libraries are composed of large numbers of peptides, oligonucleotides, or organic compounds as a mixture. These libraries are relatively easy to prepare by traditional automated synthesis methods, PCR, cloning, or proprietary synthetic methods. Of particular interest are non-peptide combinatorial libraries. Still other libraries of interest include peptide, protein, peptidomimetic, multiparallel synthetic collection, recombinatorial, and polypeptide libraries. For a review of combinatorial chemistry and libraries created therefrom, see Myers, Curr. Opin. Biotechnol. 8:701-707 (1997). Identification of modulators through use of the various libraries described herein permits modification of the candidate "hit" (or "lead") to optimize the capacity of the "hit" to modulate activity.

[000184] Still other candidate inhibitors contemplated by the invention can be designed and include soluble forms of binding partners, as well as such binding partners as chimeric, or fusion, proteins. A "binding partner" as used herein broadly encompasses non-peptide modulators, as well as such peptide modulators as neuropeptides other than natural ligands, antibodies, antibody fragments, and modified compounds comprising antibody domains that are immunospecific for the expression product of the identified nGPCR-x gene.

[000185] The polypeptides of the invention are employed as a research tool for identification, characterization and purification of interacting, regulatory proteins. Appropriate labels are incorporated into the polypeptides of the invention by various methods known in the art and the polypeptides are used to capture interacting molecules. For example, molecules are incubated with the labeled polypeptides, washed to remove unbound polypeptides, and the polypeptide complex is quantified. Data obtained using different concentrations of polypeptide are used to calculate values for the number, affinity, and association of polypeptide with the protein complex.

[000186] Labeled polypeptides are also useful as reagents for the purification of molecules with which the polypeptide interacts including, but not limited to, inhibitors. In one embodiment of affinity purification, a polypeptide is covalently coupled to a chromatography column. Cells and their membranes are extracted, and various cellular subcomponents are passed over the column. Molecules bind to the column by virtue of their affinity to the polypeptide. The polypeptide-complex is recovered from the column, dissociated and the recovered molecule is subjected to protein sequencing. This amino acid sequence is then used to identify the captured molecule or to design degenerate oligonucleotides for cloning the corresponding gene from an appropriate cDNA library.

[000187] Alternatively, compounds may be identified which exhibit similar properties to the ligand for the nGPCR-x of the invention, but which are smaller and exhibit a longer half time than the endogenous ligand in a human or animal body. When an organic compound is designed, a molecule according to the invention is used as a "lead" compound. The design of mimetics to known pharmaceutically active compounds is a well-known approach in the development of pharmaceuticals based on such "lead" compounds. Mimetic design, synthesis and testing are generally used to avoid randomly screening a large number ofmolecules for a target property. Furthermore, structural data deriving from the analysis of the deduced amino acid sequences encoded by the DNAs of the present invention are useful to design new drugs, more specific and therefore with a higher pharmacological potency.

[000188] Comparison of the protein sequence of the present invention with the sequences present in all the available databases showed a significant homology with the transmembrane portion of G protein coupled receptors. Accordingly, computer modeling can be used to develop a putative tertiary structure of the proteins of the invention based on the available information of the transmembrane domain of other proteins. Thus, novel ligands based on the predicted structure of nGPCR-x can be designed.

[000189] In a particular embodiment, the novel molecules identified by the screening methods according to the invention are low molecular weight organic molecules, in which case a composition or pharmaceutical composition can be prepared thereof for oral intake, such as in tablets. The compositions, or pharmaceutical compositions, comprising the nucleic acid molecules, vectors, polypeptides, antibodies and compounds identified by the screening methods described herein, can be prepared for any route of administration including, but not limited to, oral, intravenous, cutaneous, subcutaneous, nasal, intramuscular or intraperitoneal. The nature of the carrier or other ingredients will depend on the specific route of administration and particular embodiment of the invention to be administered. Examples of techniques and protocols that are useful in this context are, *inter alia*, found in Remington's Pharmaceutical Sciences, 16th edition, Osol, A (ed.), **1980**, which is incorporated herein by reference in its entirety.

[000190] The dosage of these low molecular weight compounds will depend on the disease state or condition to be treated and other clinical factors such as weight and condition of the human or animal and the route of administration of the compound. For treating human or animals, between approximately 0.5 mg/kg of body weight to 500 mg/kg of body weight of the compound can be administered. Therapy is typically administered at lower dosages and is continued until the desired therapeutic outcome is observed.

[000191] The present compounds and methods, including nucleic acid molecules, polypeptides, antibodies, compounds identified by the screening methods described herein, have a variety of pharmaceutical applications and may be used, for example, to treat or prevent unregulated cellular growth, such as cancer cell and tumor growth. In a particular embodiment, the present molecules are used in gene therapy. For a review of gene therapy procedures, see *e.g.* Anderson, *Science*, **1992**, *256*, 808-813, which is incorporated herein by reference in its entirety.

[000192] The present invention also encompasses a method of agonizing (stimulating) or antagonizing a nGPCR-x natural binding partner associated activity in a mammal comprising administering to said mammal an agonist or antagonist to one of the above disclosed polypeptides in an amount sufficient to effect said agonism or antagonism. One embodiment of the present invention, then, is a method of treating diseases in a mammal with an agonist or antagonist of the protein of the present invention comprises administering the agonist or antagonist to a mammal in an amount sufficient to agonize or antagonize nGPCR-x-associated functions.

[000193] In an effort to discover novel treatments for diseases, biomedical researchers and chemists have designed, synthesized, and tested molecules that modulate the function of G protein coupled receptors. Some small organic molecules form a class of compounds that modulate the function of G protein coupled receptors.

[000194] Exemplary diseases and conditions amenable to treatment based on the present invention include, but are not limited to, thyroid disorders (*e.g.* thyreotoxicosis, myxoedema); renal failure; inflammatory conditions (*e.g.*, Chron's disease); diseases related to cell differentiation and homeostasis; rheumatoid arthritis; autoimmune disorders; movement disorders; CNS disorders (*e.g.*, pain including migraine; stroke; psychotic and neurological disorders, including anxiety, mental disorder, manic depression, anxiety, generalized anxiety disorder, post-traumatic-stress disorder, depression, bipolar disorder, delirium, dementia, severe mental retardation; dyskinesias, such as Huntington's disease or Tourette's Syndrome; attention disorders including ADD and ADHD, and degenerative disorders such as Parkinson's, Alzheimer's; movement disorders, including ataxias, supranuclear palsy, *etc*); infections, such as viral infections caused by HIV-1 or HIV-2; metabolic and cardiovascular diseases and disorders (*e.g.*, type 2 diabetes, impaired glucose tolerance, dyslipidemia, obesity, anorexia, hypotension, hypertension, thrombosis, myocardial infarction, cardiomyopathies, atherosclerosis, *etc.*); proliferative diseases and cancers (*e.g.*, different cancers such as breast, colon, lung, *etc.*, and hyperproliferative disorders such as psoriasis, prostate hyperplasia, *etc.*); hormonal disorders (*e.g.*, male/female hormonal replacement, polycystic ovarian syndrome, alopecia, *etc.*); sexual dysfunction, among others.

[000195] Methods of determining the dosages of compounds to be administered to a patient and modes of administering compounds to an organism are disclosed in U.S. Application Serial No. 08/702,282, filed August 23, 1996 and International patent publication number WO 96/22976, published August 1 1996, both of which are incorporated herein by reference in their entirety, including any drawings, figures or tables. Those skilled in the art will appreciate that such descriptions are applicable to the present invention and can be easily adapted to it.

[000196] The proper dosage depends on various factors such as the type of disease being treated, the particular composition being used and the size and physiological condition of the patient. Therapeutically effective doses for the compounds described herein can be estimated initially from cell culture and animal models. For example, a dose can be formulated in animal models to achieve a circulating concentration range that initially takes into account the IC_{50} as determined in cell culture assays. The animal model data can be used to more accurately determine useful doses in humans.

[000197] Plasma half-life and biodistribution of the drug and metabolites in the plasma, tumors and major organs can also be determined to facilitate the selection of drugs most appropriate to inhibit a disorder. Such measurements can be carried out. For example, HPLC analysis can be performed on the plasma of animals treated with the drug and the location of radiolabeled compounds can be determined using detection methods such as X-ray, CAT scan and MRI. Compounds that show potent inhibitory activity in the screening assays, but have poor pharmacokinetic characteristics, can be optimized by altering the chemical structure and retesting. In this regard, compounds displaying good pharmacokinetic characteristics can be used as a model.

[000198] Toxicity studies can also be carried out by measuring the blood cell composition. For example, toxicity studies can be carried out in a suitable animal model as follows: 1) the compound is administered to mice (an untreated control mouse should also be used); 2) blood samples are periodically obtained via the tail vein from one mouse in each treatment group; and 3) the samples are analyzed for red and white blood cell counts, blood cell composition and the percent of lymphocytes versus polymorphonuclear cells. A comparison of results for each dosing regime with the controls indicates if toxicity is present.

[000199] At the termination of each toxicity study, further studies can be carried out by sacrificing the animals (preferably, in accordance with the American Veterinary Medical Association guidelines Report of the American Veterinary Medical Assoc. Panel on Euthanasia, Journal of American Veterinary Medical Assoc., 202:229-249, 1993). Representative animals from each treatment group can then be examined by gross necropsy for immediate evidence of metastasis, unusual illness or toxicity. Gross abnormalities in tissue are noted and tissues are examined

histologically. Compounds causing a reduction in body weight or blood components are less preferred, as are compounds having an adverse effect on major organs. In general, the greater the adverse effect the less preferred the compound.

[000200] For the treatment of many diseases, the expected daily dose of a hydrophobic pharmaceutical agent is between 1 to 500 mg/day, preferably 1 to 250 mg/day, and most preferably 1 to 50 mg/day. Drugs can be delivered less frequently provided plasma levels of the active moiety are sufficient to maintain therapeutic effectiveness. Plasma levels should reflect the potency of the drug. Generally, the more potent the compound the lower the plasma levels necessary to achieve efficacy.

[000201] As discussed above, it is well known that GPCRs are expressed in many different tissues and regions, including in the brain. nGPCR-x mRNA transcripts may found in many other tissues, including, but not limited to peripheral blood lymphocytes, pancreas, ovary, uterus, testis, salivary gland, kidney, adrenal gland, liver, bone marrow, prostate, fetal liver, colon, muscle, and fetal brain, and may be found in many other tissues. Within the brain, nGPCR-x mRNA transcripts may be found in many tissues, including, but not limited to, frontal lobe, hypothalamus, pons, cerebellum, caudate nucleus, and medulla.

[000202] Sequences selected from the group consisting of SEQ ID NO:1 to SEQ ID NO:128 will, as detailed above, enable screening the endogenous neurotransmitters/hormones/ligands which activate, agonize, or antagonize nGPCR-x and for compounds with potential utility in treating disorders including, but not limited to, thyroid disorders (*e.g.* thyreotoxicosis, myxoedema); renal failure; inflammatory conditions (*e.g.*, Chron's disease); diseases related to cell differentiation and homeostasis; rheumatoid arthritis; autoimmune disorders; movement disorders; CNS disorders (*e.g.*, pain including schizophrenia, migraine; stroke; psychotic and neurological disorders, including anxiety, mental disorder, manic depression, anxiety, generalized anxiety disorder, post-traumatic-stress disorder, depression, bipolar disorder, delirium, dementia, severe mental retardation; dyskinesias, such as Huntington's disease or Tourette's Syndrome; attention disorders including ADD and ADHD, and degenerative disorders such as Parkinson's, Alzheimer's; movement disorders, including ataxias, supranuclear palsy, *etc.*); infections, such as viral infections caused by HIV-1 or HIV-2; metabolic and cardiovascular diseases and disorders (*e.g.*, type 2 diabetes, impaired glucose tolerance, dyslipidemia, obesity, anorexia, hypotension, hypertension, thrombosis, myocardial infarction, cardiomyopathies, atherosclerosis, *etc.*); proliferative diseases and cancers (*e.g.*, different cancers such as breast, colon, lung, *etc.*, and hyperproliferative disorders such as psoriasis, prostate hyperplasia, *etc.*); hormonal disorders (*eg.*, male/female hormonal replacement, polycystic ovarian syndrome, alopecia, *etc.*); sexual dysfunction, among others.

[000203] For example, nGPCR-x may be useful in the treatment of respiratory ailments such as asthma, where T cells are implicated by the disease. Contraction of airway smooth muscle is stimulated by thrombin. Cicala *et al* (1999) Br J Pharmacol 126:478-484. Additionally, in bronchiolitis obliterans, it has been noted that activation of thrombin receptors may be deleterious. Hauck *et al.* (1999) Am J Physiol 277:L22-L29. Furthermore, mast cells have also been shown to have thrombin receptors. Cirino *et al* (1996) J Exp Med 183:821-827. nGPCR-x may also be useful in remodeling of airway structure s in chronic pulmonary inflammation via stimulation of fibroblast procollagen synthesis. See, e.g., Chambers *et al.* (1998) Biochem J 333:121-127; Trejo *et al.* (1996) J Biol Chem 271:21536-21541.

[000204] In another example, increased release of sCD40L and expression of CD40L by T cells after activation of thrombin receptors suggests that nGPCR-x may be useful in the treatment of unstable angina due to the role of T cells and inflammation. See Aukrust *et al.* (1999) Circulation 100:614-620.

[000205] A further example is the treatment of inflammatory diseases, such as psoriasis, inflammatory bowel disease, multiple sclerosis, rheumatoid arthritis, and thyroiditis. Due to the tissue expression profile of nGPCR-x, inhibition of thrombin receptors may be beneficial for these diseases. See, *e.g.*, Morris *et al.* (1996) Ann Rheum Dis 55:841-843. In addition to T cells, NK cells and monocytes are also critical cell types which contribute to the pathogenesis of these diseases. See, e.g., Naldini & Carney (1996) Cell Immunol 172:35-42; Hoffman & Cooper (1995) Blood Cells Mol Dis 21:156-167; Colotta *et al.* (1994) Am J Pathol 144:975-985.

[000206] Expression of nGPCR-x in bone marrow and spleen may suggest that it may play a role in the proliferation of hematopoietic progenitor cells. See DiCuccio *et al.* (1996) Exp Hematol 24:914-918.

[000207] As another example, nGPCR-x may be useful in the treatment of acute and/or traumatic brain injury. Astrocytes have been demonstrated to express thrombin receptors. Activation of thrombin receptors may be involved in astrogliosis following brain injury. Therefore, inhibition of receptor activity may be beneficial for limiting neuroinflammation. Scar formation mediated by astrocytes may also be limited by inhibiting thrombin receptors. See, *e.g*, Pindon *et al.* (1998) Eur J Biochem 255:766-774; Ubl & Reiser. (1997) Glia 21:361-369; Grabham & Cunningham (1995) J Neurochem 64:583-591.

[000208] nGPCR-x receptor activation may mediate neuronal and astrocyte apoptosis and prevention of neurite outgrowth. Inhibition would be beneficial in both chronic and acute brain injury. See, *e.g.*, Donovan *et al.* (1997) J Neurosci 17:5316-5326; Turgeon *et al* (1998) J Neurosci 18:6882-6891; Smith-Swintosky *et al.* (1997) J Neurochem 69:1890-1896; Gill *et al.* (1998) Brain Res 797:321-327; Suidan *et al.* (1996) Semin Thromb Hemost 22:125-133.

[000209] The attached Sequence Listing contains the sequences of the polynucleotides and polypeptides of the invention and is incorporated herein by reference in its entirety.

Methods of Screening Human Subjects

[000210] Thus in yet another embodiment, the invention provides genetic screening procedures that entail analyzing a person's genome -- in particular their alleles for the nGPCR-x of the invention -- to determine whether the individual possesses a genetic characteristic found in other individuals that are considered to be afflicted with, or at risk for, developing a mental disorder or disease of the brain that is suspected of having a hereditary component. For example, in one embodiment, the invention provides a method for determining a potential for developing a disorder affecting the brain in a human subject comprising the steps of analyzing the coding sequence of one or more nGPCR-x genes from the human subject; and determining development potential for the disorder in said human subject from the analyzing step.

[000211] More particularly, the invention provides a method of screening a human subject to diagnose a disorder affecting the brain or genetic predisposition therefor, comprising the steps of: (a) assaying nucleic acid of a human subject to determine a presence or an absence of a mutation altering the amino acid sequence, expression, or biological activity of at least one seven transmembrane receptor that is expressed in the brain, wherein the seven transmembrane receptor comprises an amino acid sequence selected from the group consisting of SEQ ID NO:1 to SEQ ID NO:128, or an allelic variant thereof, and wherein the nucleic acid corresponds to the gene encoding the seven transmembrane receptor; and (b) diagnosing the disorder or predisposition from the presence or absence of said mutation, wherein the presence of a mutation altering the amino acid sequence, expression, or biological activity of allele in the nucleic acid correlates with an increased risk of developing the disorder.

[000212] By "human subject" is meant any human being, human embryo, or human fetus. It will be apparent that methods of the present invention will be of particular interest to individuals that have themselves been diagnosed with a disorder affecting the brain or have relatives that have been diagnosed with a disorder affecting the brain.

[000213] By "screening for an increased risk" is meant determination of whether a genetic variation exists in the human subject that correlates with a greater likelihood of developing a disorder affecting the brain than exists for the human population as a whole, or for a relevant racial or ethnic human sub-population to which the individual belongs. Both positive and negative determinations (i.e., determinations that a genetic predisposition marker is present or is absent) are intended to fall within the scope of screening methods of the invention. In preferred embodiments, the presence of a mutation altering the sequence or expression of at least one nGPCR-x seven transmembrane receptor allele in the nucleic acid is correlated with an

increased risk of developing mental disorder, whereas the absence of such a mutation is reported as a negative determination.

[000214] The "assaying" step of the invention may involve any techniques available for analyzing nucleic acid to determine its characteristics, including but not limited to well-known techniques such as single-strand conformation polymorphism analysis (SSCP) [Orita *et al., Proc Natl. Acad. Sci. USA, 86*: 2766-2770 (1989)]; heteroduplex analysis [White *et al., Genomics, 12*: 301-306 (1992)]; denaturing gradient gel electrophoresis analysis [Fischer *et al., Proc. Natl. Acad. Sci. USA, 80*: 1579-1583 (1983); and Riesner *et al., Electrophoresis, 10*: 377-389 (1989)]; DNA sequencing; RNase cleavage [Myers *et al., Science, 230*: 1242-1246 (1985)]; chemical cleavage of mismatch techniques [Rowley *et al., Genomics, 30*: 574-582 (1995); and Roberts *et al., Nucl. Acids Res., 25*: 3377-3378 (1997)]; restriction fragment length polymorphism analysis; single nucleotide primer extension analysis [Shumaker *et al., Hum. Mutat., 7*: 346-354 (1996); and Pastinen *et al., Genome Res., 7*: 606-614 (1997)]; 5' nuclease assays [Pease *et al., Proc. Natl. Acad. Sci. USA, 91*:5022-5026 (1994)]; DNA Microchip analysis [Ramsay, G.,*Nature Biotechnology, 16*: 40-48 (1999); and Chee *et al.*, U.S. Patent No. 5,837,832]; and ligase chain reaction [Whiteley *et al.*, U.S. Patent No. 5,521,065]. [See generally, Schafer and Hawkins, *Nature Biotechnology, 16*: 33-39 (1998).] All of the foregoing documents are hereby incorporated by reference in their entirety.

[000215] Thus, in one preferred embodiment involving screening nGPCR-x sequences, for example, the assaying step comprises at least one procedure selected from the group consisting of: (a) determining a nucleotide sequence of at least one codon of at least one nGPCR-x allele of the human subject; (b) performing a hybridization assay to determine whether nucleic acid from the human subject has a nucleotide sequence identical to or different from one or more reference sequences; (c) performing a polynucleotide migration assay to determine whether nucleic acid from the human subject has a nucleotide sequence identical to or different from one or more reference sequences; and (d) performing a restriction endonuclease digestion to determine whether nucleic acid from the human subject has a nucleotide sequence identical to or different from one or more reference sequences.

[000216] In a highly preferred embodiment, the assaying involves sequencing of nucleic acid to determine nucleotide sequence thereof, using any available sequencing technique. [See, *e.g.*, Sanger *et al., Proc. Natl. Acad. Sci. (USA), 74*: 5463-5467 (1977) (dideoxy chain termination method); Mirzabekov, *TIBTECH, 12*: 27-32 (1994) (sequencing by hybridization); Drmanac *et al., Nature Biotechnology, 16*: 54-58 (1998); U.S. Patent No. 5,202,231; and *Science, 260*: 1649-1652 (1993) (sequencing by hybridization); Kieleczawa *et al., Science, 258*: 1787-1791 (1992) (sequencing by primer walking); (Douglas *et al., Biotechniques, 14*: 824-828 (1993)

(Direct sequencing of PCR products); and Akane *et al., Biotechniques 16*: 238-241 (1994); Maxam and Gilbert, *Meth. Enzymol., 65*: 499-560 (1977) (chemical termination sequencing), all incorporated herein by reference.] The analysis may entail sequencing of the entire nGPCR gene genomic DNA sequence, or portions thereof; or sequencing of the entire seven transmembrane receptor coding sequence or portions thereof. In some circumstances, the analysis may involve a determination of whether an individual possesses a particular allelic variant, in which case sequencing of only a small portion of nucleic acid -- enough to determine the sequence of a particular codon characterizing the allelic variant -- is sufficient. This approach is appropriate, for example, when assaying to determine whether one family member inherited the same allelic variant that has been previously characterized for another family member, or, more generally, whether a person's genome contains an allelic variant that has been previously characterized and correlated with a mental disorder having a heritable component.

[000217] In another highly preferred embodiment, the assaying step comprises performing a hybridization assay to determine whether nucleic acid from the human subject has a nucleotide sequence identical to or different from one or more reference sequences. In a preferred embodiment, the hybridization involves a determination of whether nucleic acid derived from the human subject will hybridize with one or more oligonucleotides, wherein the oligonucleotides have nucleotide sequences that correspond identically to a portion of the nGPCR-x gene sequence taught herein, or that correspond identically except for one mismatch. The hybridization conditions are selected to differentiate between perfect sequence complementarity and imperfect matches differing by one or more bases. Such hybridization experiments thereby can provide single nucleotide polymorphism sequence information about the nucleic acid from the human subject, by virtue of knowing the sequences of the oligonucleotides used in the experiments.

[000218] Several of the techniques outlined above involve an analysis wherein one performs a polynucleotide migration assay, *e.g.*, on a polyacrylamide electrophoresis gel (or in a capillary electrophoresis system), under denaturing or non-denaturing conditions. Nucleic acid derived from the human subject is subjected to gel electrophoresis, usually adjacent to (or co-loaded with) one or more reference nucleic acids, such as reference GPCR-x encoding sequences having a coding sequence identical to all or a portion of SEQ ID NOS: 1 to 110 (or identical except for one known polymorphism). The nucleic acid from the human subject and the reference sequence(s) are subjected to similar chemical or enzymatic treatments and then electrophoresed under conditions whereby the polynucleotides will show a differential migration pattern, unless they contain identical sequences. [See generally Ausubel *et al.* (eds.), *Current Protocols in Molecular Biology*, New York: John Wiley & Sons, Inc. (1987-1999); and

Sambrook *et al.*, (eds.), Molecular Cloning, *A Laboratory Manual*, Cold Spring Harbor, New York: Cold Spring Harbor Laboratory Press (1989), both incorporated herein by reference in their entirety.]

[000219] In the context of assaying, the term "nucleic acid of a human subject" is intended to include nucleic acid obtained directly from the human subject (*e.g.*, DNA or RNA obtained from a biological sample such as a blood, tissue, or other cell or fluid sample); and also nucleic acid derived from nucleic acid obtained directly from the human subject. By way of non-limiting examples, well known procedures exist for creating cDNA that is complementary to RNA derived from a biological sample from a human subject, and for amplifying (*e.g*, via polymerase chain reaction (PCR)) DNA or RNA derived from a biological sample obtained from a human subject. Any such derived polynucleotide which retains relevant nucleotide sequence information of the human subject's own DNA/RNA is intended to fall within the definition of "nucleic acid of a human subject" for the purposes of the present invention.

[000220] In the context of assaying, the term "mutation" includes addition, deletion, and/or substitution of one or more nucleotides in the GPCR gene sequence (*e.g.*, ascompared to the seven transmembrane receptor-encoding sequences set forth of SEQ ID NO:1 to SEQ ID NO:128, and other polymorphisms that occur in introns (where introns exist) and that are identifiable via sequencing, restriction fragment length polymorphism, or other techniques. The various activity examples provided herein permit determination of whether a mutation modulates activity of the relevant receptor in the presence or absence of various test substances.

[000221] In a related embodiment, the invention provides methods of screening a person's genotype with respect to the nGPCR-x of the invention, and correlating such genotypes with diagnoses for disease or with predisposition for disease (for genetic counseling). For example, the invention provides a method of screening for an nGPCR-x hereditary mental disorder genotype in a human patient, comprising the steps of: (a) providing a biological sample comprising nucleic acid from the patient, the nucleic acid including sequences corresponding to said patient's nGPCR-x alleles; (b) analyzing the nucleic acid for the presence of a mutation or mutations; (c) determining a nGPCR-x genotype from the analyzing step; and (d) correlating the presence of a mutation in an nGPCR-x allele with a hereditary mental disorder genotype. In a preferred embodiment, the biological sample is a cell sample containing human cells that contain genomic DNA of the human subject. The analyzing can be performed analogously to the assaying described in preceding paragraphs. For example, the analyzing comprises sequencing a portion of the nucleic acid (e.g., DNA or RNA), the portion comprising at least one codon of the nGPCR-x alleles.

[000222] Although more time consuming and expensive than methods involving nucleic acid analysis, the invention also may be practiced by assaying one or more proteins of a human subject to determine the presence or absence of an amino acid sequence variation in GPCR protein from the human subject. Such protein analyses may be performed, *e.g.*, by fragmenting GPCR protein via chemical or enzymatic methods and sequencing the resultant peptides; or by Western analyses using an antibody having specificity for a particular allelic variant of the GPCR.

[000223] The invention also provides materials that are useful for performing methods of the invention. For example, the present invention provides oligonucleotides useful as probes in the many analyzing techniques described above. In general, such oligonucleotide probes comprise 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, or 50 nucleotides that have a sequence that is identical, or exactly complementary, to a portion of a human GPCR gene sequence taught herein (or allelic variant thereof), or that is identical or exactly complementary except for one nucleotide substitution. In a preferred embodiment, the oligonucleotides have a sequence that corresponds in the foregoing manner to a human GPCR coding sequence taught herein, and in particular, the coding sequences set forth in SEQ ID NO:1 to SEQ ID NO:128. In one variation, an oligonucleotide probe of the invention is purified and isolated. In another variation, the oligonucleotide probe is labeled, *e.g.*, with a radioisotope, chromophore, or fluorophore. In yet another variation, the probe is covalently attached to a solid support. [See generally Ausubel *et al.* and Sambrook *et al.*, *supra.*]

[000224] In a related embodiment, the invention provides kits comprising reagents that are useful for practicing methods of the invention. For example, the invention provides a kit for screening a human subject to diagnose a mental disorder or a genetic predisposition therefor, comprising, in association: (a) an oligonucleotide useful as a probe for identifying polymorphisms in a human nGPCR-x seven transmembrane receptor gene, the oligonucleotide comprising 6-50 nucleotides that have a sequence that is identical or exactly complementary to a portion of a human nGPCR-x gene sequence or nGPCR-x coding sequence, except for one sequence difference selected from the group consisting of a nucleotide addition, a nucleotide deletion, or nucleotide substitution; and (b) a media packaged with the oligonucleotide containing information identifying polymorphisms identifiable with the probe that correlate with mental disorder or a genetic predisposition therefor. Exemplary information-containing media include printed paper package inserts or packaging labels; and magnetic and optical storage media that are readable by computers or machines used by practitioners who perform genetic screening and counseling services. The practitioner uses the information provided in the media to correlate the

results of the analysis with the oligonucleotide with a diagnosis. In a preferred variation, the oligonucleotide is labeled.

[000225] In still another embodiment, the invention provides methods of identifying those allelic variants of GPCRs of the invention that correlate with mental disorders. For example, the invention provides a method of identifying a seven transmembrane allelic variant that correlates with a mental disorder, comprising steps of: (a) providing a biological sample comprising nucleic acid from a human patient diagnosed with a mental disorder, or from the patient's genetic progenitors or progeny; (b) analyzing the nucleic acid for the presence of a mutation or mutations in at least one seven transmembrane receptor that is expressed in the brain, wherein the at least one seven transmembrane receptor comprises an amino acid sequence selected from the group consisting of SEQ ID NO:1 to SEQ ID NO:128 or an allelic variant thereof, and wherein the nucleic acid includes sequence corresponding to the gene or genes encoding the at least one seven transmembrane receptor; (c) determining a genotype for the patient for the at least one seven transmembrane receptor from said analyzing step; and (d) identifying an allelic variant that correlates with the mental disorder from the determining step. To expedite this process, it may be desirable to perform linkage studies in the patients (and possibly their families) to correlate chromosomal markers with disease states. The chromosomal localization data provided herein facilitates identifying an involved nGPCR with a chromosomal marker.

[000226] The foregoing method can be performed to correlate the nGPCR-x of the invention to a number of disorders having hereditary components that are causative or that predispose persons to the disorder. For example, in one preferred variation, the disorder is a mental disorder.

[000227] Also contemplated as part of the invention are polynucleotides that comprise the allelic variant sequences identified by such methods, and polypeptides encoded by the allelic variant sequences, and oligonucleotide and oligopeptide fragments thereof that embody the mutations that have been identified. Such materials are useful in *in vitro* cell-free and cell-based assays for identifying lead compounds and therapeutics for treatment of the disorders. For example, the variants are used in activity assays, binding assays, and assays to screen for activity modulators described herein. In one preferred embodiment, the invention provides a purified and isolated polynucleotide comprising a nucleotide sequence encoding a nGPCR-x receptor allelic variant identified according to the methods described above; and an oligonucleotide that comprises the sequences that differentiate the allelic variant from the nGPCR-x sequences set forth in SEQ ID NO:1 to SEQ ID NO:128. The invention also provides a vector comprising the polynucleotide (preferably an expression vector); and a host cell transformed or transfected with the polynucleotide or vector. The invention also provides an isolated cell line that is expressing the allelic variant nGPCR-x polypeptide; purified cell membranes from such cells; purified

polypeptide; and synthetic peptides that embody the allelic variation amino acid sequence. In one particular embodiment, the invention provides a purified polynucleotide comprising a nucleotide sequence encoding a nGPCR-x seven transmembrane receptor protein of a human that is affected with a mental disorder; wherein said polynucleotide hybridizes to the complement of a sequence selected from the group consisting of SEQ ID NO:1 to SEQID NO:128 under the following hybridization conditions: (a) hybridization for 16 hours at 42°C in a hybridization solution comprising 50% formamide, 1% SDS, 1 M NaCl, 10% dextran sulfate and (b) washing 2 times for 30 minutes at 60°C in a wash solution comprising 0.1x SSC and 1% SDS; and wherein the polynucleotide encodes a nGPCR-x amino acid sequence that differs from a sequence selected from the group consisting of SEQ ID NO:129 to SEQ ID NO:257, by at least one residue.

[000228] An exemplary assay for using the allelic variants is a method for identifying a modulator of nGPCR-x biological activity, comprising the steps of: (a) contacting a cell expressing the allelic variant in the presence and in the absence of a putative modulator compound; (b) measuring nGPCR-x biological activity in the cell; and (c) identifying a putative modulator compound in view of decreased or increased nGPCR-x biological activity in the presence versus absence of the putative modulator.

[000229] Additional features of the invention will be apparent from the following Examples. Examples 1 and 2 are actual while the remaining Examples are prophetic. Additional features and variations of the invention will be apparent to those skilled in the art from the entirety of this application, including the detailed description, and all such features are intended as aspects of the invention. Likewise, features of the invention described herein can be re-combined into additional embodiments that also are intended as aspects of the invention, irrespective of whether the combination of features is specifically mentioned above as an aspect or embodiment of the invention. Also, only such limitations which are described herein as critical to the invention should be viewed as such; variations of the invention lacking limitations which have not been described herein as critical are intended as aspects of the invention.

EXAMPLES

EXAMPLE 1: IDENTIFICATION OF nGPCR-X

A. Database search

[000230] The Celera database was searched using known GPCR receptors as query sequences to find patterns suggestive of novel G protein-coupled receptors. Positive hits were further analyzed with the GCG program BLAST to determine which ones were the most likely

candidates to encode G protein-coupled receptors, using the standard (default) alignment produced by BLAST as a guide.

[000231] Briefly, the BLAST algorithm, which stands for Basic Local Alignment Search Tool is suitable for determining sequence similarity (Altschul *et al.*, J. Mol. Biol., 1990, 215, 403-410, which is incorporated herein by reference in its entirety). Software for performing BLAST analyses is publicly available through the National Center for Biotechnology Information (http://www.ncbi.nlm.nih.gov/). This algorithm involves first identifying high scoring sequence pair (HSPs) by identifying short words of length W in the query sequence that either match or satisfy some positive-valued threshold score T when aligned with a word of the same length in a database sequence. T is referred to as the neighborhood word score threshold (Altschul*et al.*, *supra*). These initial neighborhood word hits act as seeds for initiating searchesto find HSPs containing them. The word hits are extended in both directions along each sequence for as far as the cumulative alignment score can be increased. Extension for the word hits in each direction are halted when: 1) the cumulative alignment score falls off by the quantity X from its maximum achieved value; 2) the cumulative score goes to zero or below, due to the accumulation of one or more negative-scoring residue alignments; or 3) the end of either sequence is reached. The Blast algorithm parameters W, T and X determine the sensitivity and speed of the alignment. The Blast program uses as defaults a word length (W) of 11, the BLOSUM62 scoring matrix (see Henikoff et al., Proc. Natl. Acad. Sci. USA, 1992, 89, 10915-10919, which is incorporated herein by reference in its entirety) alignments (B) of 50, expectation (E) of 10, M=5, N=4, and a comparison of both strands.

[000232] The BLAST algorithm (Karlin *et al.*, Proc. Natl. Acad. Sci. USA, 1993, 90, 5873-5787, which is incorporated herein by reference in its entirety) and Gapped BLAST perform a statistical analysis of the similarity between two sequences. One measure of similarity provided by the BLAST algorithm is the smallest sum probability (P(N)), which provides an indication of the probability by which a match between two nucleotide or amino acid sequences would occur by chance. For example, a nucleic acid is considered similar to a GPCR gene or cDNA if the smallest sum probability in comparison of the test nucleic acid to a GPCR nucleic acid is less than about 1, preferably less than about 0.1, more preferably less than about 0.01, and most preferably less than about 0.001.

[000233] Homology searches are performed with the program BLAST version 2.08. A collection of 340 query amino acid sequences derived from GPCRs was used to search the genomic DNA sequence using TBLASTN and alignments with an E-value lower than 0.01 were collected from each BLAST search. The amino acid sequences have been edited to remove regions in the sequence that produce non-significant alignments with proteins that are not related to GPCRs.

[000234] Multiple query sequences may have a significant alignment to the same genomic region, although each alignment may not cover exactly the same DNA region. A procedure is used to determine the region of maximum common overlap between the alignments from several query sequences. This region is called the consensus DNA region. The procedure for determining this consensus involves the automatic parsing of the BLAST output files using the program MSPcrunch to produce a tabular report. From this tabular report the start and end of each alignment in the genomic DNA is extracted. This information is used by a PERL script to derive the maximum common overlap. These regions are reported in the form of a unique sequence identifier, a start and the end position in the sequence. The sequences defined by these regions were extracted from the original genomic sequence file using the program fetchdb.

[000235] The consensus regions are assembled into a non-redundant set by using the program phrap. After assembly with phrap a set of contigs and singletons were defined as candidate DNA regions coding for nGPCRs. These sequences were then submitted for further sequence analysis.

[000236] Further sequence analysis involves the removal of sequences previously isolated and removal of sequences that are related to olfactory GPCR's.

[000237] *n*GPRCR-x cDNAs were sequenced directly using an ABI377 fluorescence-based sequencer (Perkin-Elmer/Applied Biosystems Division, PE/ABD, Foster City, CA) and the ABI PRISM™ Ready Dye-Deoxy Terminator kit with Taq FS™ polymerase. Each ABI cycle sequencing reaction contained about 0.5 µg of plasmid DNA. Cycle-sequencing was performed using an initial denaturation at 98°C for 1 minute, followed by 50 cycles using the following parameters: 98°C for 30 seconds, annealing at 50°C for 30 seconds, and extension at 60°C for 4 minutes. Temperature cycles and times were controlled by a Perkin-Elmer 9600 thermocycler. Extension products were purified using Centriflex™ gel filtration cartridges (Advanced Genetic Technologies Corp., Gaithersburg, MD). Each reaction product was loaded by pipette onto the column, which is then centrifuged in a swinging bucket centrifuge (Sorvall model RT6000B tabletop centrifuge) at 1500 x *g* for 4 minutes at room temperature. Column-purified samples were dried under vacuum for about 40 minutes and then dissolved in 5µl of a DNA loading solution (83% deionized formamide, 8.3mM EDTA, and 1.6 mg/ml Blue Dextran). The samples were then heated to 90°C for three minutes and loaded into the gel sample wells for sequence analysis using the ABI377 sequencer. Sequence analysis was performed by importing ABI377 files into the Sequencer program (Gene Codes, Ann Arbor, MI). Generally, sequence reads of 700 bp were obtained. Potential sequencing errors were minimized by obtaining sequence information from both DNA strands and by re-sequencing difficult areas using primers annealing at different locations until all sequencing ambiguities were removed.

[000238] The following Table 5 contains the sequences of the polynucleotides and polypeptides of the invention. The transmembrane domains within the polypeptide sequence are identified by underlining.

Table 5

The following DNA sequence Seq-2227 <SEQ ID NO. 1> was identified in *H. sapiens*:

AATGTGGAAGTCATCAGCATCAAGGTATTTGAGACCATGAGACCAGGGGAGGTCACTAAGGGACTGAGTGT
GGAAAGAAAAGAAAAAGTTCCAGGACTGACCCCTGAGCCGTCCAGGGTCAGGAGTCAAAATCATGAAAAGC
AATGAAAAGAAATGAAGCCAAGAGCAGCCAGTGCGATGAGAAGAAAACTGAGTGGTGCCCTGGAAGCCAGG
GAAGAACATGTTTCCAGGAAGGAGGGAGTGAACAGGAGGATGCCGCTGACACATCGGGTACCGTGAAGACA
GAACTGAACTGAGCAGGCTGGTTAGCTAGTGGAGGGCATTAGTGAGCTGGGAAGCTGGTCAGTTGAGTCGG
GGTAAAAGCTGATGGCAGGAGGTTCCAGAGGGAATGGGAGAAGATAAATCGGAAGAATGGCTATAGCCCGC
TGAAGGGAAGGAGAGAGGTAGAAGTGGGAGTGGGAGAGGAAAGAGGAACAAGAGGTTTCTGGTTTTGTTAT
GTAAGATGGAGGAAATGTGCTTATGAATAAGCTAAAAAAATGCTGGTGGCTGATGGATAATGTCTAATAGG
GAGG

The following amino acid sequence <SEQ ID NO. 129> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 1:

LPIRHYPSATSIFLAYSAHFLHLTQNQKPLVPLSSPTPTSTSLLPFSGLPFFRFIFSHSLWNLLPSAFTPT
QLTSFPAHCPPLANQPAQFSSVFTVPDVSAASSCSLPPSWKHVWLPGHHSVFFSSHWLLLASFLFIAFHDF
DSPWTAQGSVLELFLFFPHSVPPPLVSWSQIPCLPH

The following DNA sequence Seq-2228 SEQ ID NO. 2> was identified in *H. sapiens*:

TTGAATTCAGAATGTTATAATTTGTGCTACAATCAGTTGTCTAAAAGCTATGTTTATACCTATGCCTATTT
CTTTTGTGACTTAAATCTTGGAGGCCAGCCATATTTAGTTATTTTTGTAAAAGTTACCAAATTACAATATT
AGGCACATTTTTCAAAATGATGCTCTCGTCTTCTTATTATGCTTGGGTCGTTTATAATATATTGAGGTTTT
GCAAAAACAAACTGATGTAAGATACAGTATGCATTATCTTACATCATACATACATACATACATATATATGA
AAAGGAGAGAGAGAGAGAGAGACAGTAATAGAGATATCTATGAAATTGGAATCAGGTTAAACATATTTCAA
CTGACCCTAAATTCCTTAAAAATATTTCTTTGTAGGTATTCTGATTTAAACCACTAGTTTAATGAAATGCA
ACCACTAATTAGGGTTACTCTGTGTTATTCTTACAGTGATTCATTCTTCTAAGTTCCAAACTCCTCAAGAT
ATTTGTGTGTCTATGTATTTTTTCTCTGTAAGAGACAATTTTGGGTATTCTTAATTAAAAGCAGCCACTGT
CACAGTAAGAATAAACACTATCAGAATGTTGGGGAGGGAGGA

The following amino acid sequence <SEQ ID NO. 130> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 2:

LNSECYNLCYNQLSKSYVYTYAYFFCDLNLGGQPYLVIFVKVTKLQYAHFSKCSRLLIMLGSFIIYGFAKT
NCKIQYALSYIIHTYIHIYEKERERERQRYLNWNQVKHISTDPKFLKNISLVFFKPLVNATTNGYSVLFLQ
FILLSSKLLKIFVCLCIFSLETILGILNKQPLSQETLSECWGGR

The following DNA sequence Seq-2229 <SEQ ID NO. 3> was identified in *H. sapiens*:

CTTTGGTGGTCTCTTACACGGATGCATGAAACACACCTCATGTAAATTGAAAATAAACAAACTCGGACTAC
CCTCTTTGGGTCCCCTCCCTTTCTATGGGAGCTCTGTTTTCACTCTATTAAATCTTGCAACTGTACTCTTC
TGGTCTGTGTTTGTTATGGCTGGAGCTGAGTTTTCGCTCGCTGTCCACCACTGCTGTTTGCTGCCATCGCA
GACCCGCTGCTGACTTCCATCCCTCTCAATCCGGCAGAGTGTCCGCTGTGCTCCTGATCCAGCAAGTTGCC
CATTGCCGTTCCTGATCGGGCTAAAGGCTTGCCATTGTTCCTGCACGGCTAAGCGCCCGGGTGCGTCCTAA
TCGAGCTCAATACTAGTCACTGGGTTCTGTGGGTTCTCTTCCGTGACCCACGGCTTCTAATAGAGCTCTAA
CACTCACCACATGGCTCAAG

The following amino acid sequence <SEQ ID NO. 131> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 3:

FGGLLHGCMKHTSCKLKINKLGLPSLGPLPFYGSSVFTLLNLATVLFWSVFVMAGAEFSLAVHHCCLLPSQ
TRCLPSLSIRQSVRCAPDPASCPLPFLIGLKACHCSCTAKRPGASSSSILVTGFCGFSSVTHGFSSNTHHM

AQ

The following DNA sequence Seq-2280 <SEQ ID NO. 4> was identified in *H. sapiens*:

TCTGCAAATTTAAGATTATTCCAGTATAAAAAATTGTCAAAAACACTAATAATAAGAAGGCCCAAAAGGTG
AAACAGATATTGGCAAAGCTCTTGTGGTATGAGTAGAGGTACAGGGCCTGAGTCCTGACTGCTCAGCCTCT
TCTCACTCCTCACTCCCTTCCAGGCTGGCTCCCTCCTTCCCCAGGTCCCCAGGGTTCTCTGTCACATATTC
TGAAAAGTACTGCCCTGCAGAACTAAATGCAAGCTCCTCAACATATCTTCTGGGGCCCTTCATATTCTTAC
CCTTGGCTAGCTTTCATCTTCATCATCTGGTGACCTCTTGCCTGCTATATGTATTTCTGTATTTATTACCT
TCATATATTTTGAAGGCACTTTTTTTCCTCAAGCAGATCCTGACCTTCTTGTTGATTTTGAACATGCTACT
TTTTTCAGCTTGGAAGACCATTCTCAAGCTTACTCACCCTCAAAAACTCTTCAAAAATCATCTTAGAATTC
AGCTTAAGAGTGAGCCTTCTCTTGAAAGACTCTAAGGGAAAGGGACACCTTTCTGAAATGTTTCTACAATA
GCA

The following amino acid sequence <SEQ ID NO. 132> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 4:

LQIDYSSIKNCQKHEGPKGETDIGKALVVVEVQGLSPDCSASSHSSLPSRLAPSFPRSPGFSVTYSEKYCP
AELNASSSTYLLGPFIFLPLASFHLHHLVTSCLLYVFLYLLPSYILKALFFLKQILTFLLILNMLLFSAWK
TILKLTHPQKLFKNHLRIQLKSEPSLERLGKGTPFNVSTIA

The following DNA sequence Seq-2281 <SEQ ID NO. 5> was identified in *H. sapiens*:

CGTTTTCCTACTATGGTGCTGATTAGTTTTTTGGTAAGATTCTTGATCACAGAAGATATCAAATACACAGA
CTGAAGTTCAACACTTATTTTGAAGCTAGAAAATAAAAATATATATACATTCTTGGAATAATCTATTGCAT
ACATACAGGGTGAAAAAAATGAAGTAACTTCATAAAACAGTATCCATTTGTAAAATTCACTAGAGAATTCC
AGGGTATTTCCATGGAACTATGCATTGTCAAGTTTTTAATTAGTCACACTAATTTCCCCCTTTGGTGTTAA
CTATCAAAGCATACTCAAATCTTCCTCATTGGCATTACACATTGGAGGTGCTCAATAAATGTATGTTGGAC
TTCAGTGTGGTGTTCTGCTAAGTACTTAAAATTCAAT

The following amino acid sequence <SEQ ID NO. 133> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 5:

IEFVLSRTPHSPTYIYAPPMCNANEEDLSMLLTPKGEISVTNKLDNAFHGNTLEFSSEFYKWILFYEVTSF
FSPCMYAIDYSKNVYIFLFSSFKISVELQSVYLISSVIKNLTKKLISTIVGK

The following DNA sequence Seq-2282 <SEQ ID NO. 6> was identified in *H. sapiens*:

AGGGCCCTCATCCCACTTGATGATTATGGTTTTCTTTGCTCAGAGGAAACTAAGGTCTAGCTCCCTGCTAA
CGCAGCCTTTGGGAAGCCAACACTTTCACCCGAGAACCCTGGAATCCGGCCCCTCTCAGAGGCCCGGGAAG
GCAGTGGGGCTTGGCAGGGCTACCCGTTCTGAATTCATGTGCACCGGACTGGGTCCCCTGGAGCTACGCC

The following amino acid sequence <SEQ ID NO. 134> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 6:

GPHPTLWFSLLRGNGLAPCRSLWEANTFTREPWNPAPLRGPGRQWGLAGLPVLNSCAPDWVPWSYA

The following DNA sequence Seq-2283 <SEQ ID NO. 7> was identified in *H. sapiens*:

AAACAGCATTTTCATGAAAAATGTTCTCACCCTCGTTGTGCTAGTTCGTGGTATCTTTTTCTTCCAGGCTT
ATTCCTTCCCAAATGACTACAGTTTTTGCTGGCATTTCTCTGAAGGTATACTTGAGATCTCTTTAAGAGTC
AGAAAAGCTACCTGAAATTGCAGGCAGCTTCCTGTTGGGCTCACGTTTTGCAGAATCCACGCTTGGTGTGC
AGAAGGTGGGCAAGGTGTTTGAAAAAACAGGAAGCACCTGTGAATGTGTGAATTTATTTCTGGAAGCAGAA
GGCTCCCTCTGAGATGGCTCTAGATGCTTCCTGCTGTTCCACCTATGAGCATTTTGCAAGGCCTTTCAGTA
CTTTGGGGCTATGAACAGGCTTCCGAATGGCAGGATTATTTGGAAAATCTGGGA

The following amino acid sequence <SEQ ID NO. 135> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 7:

NSIFMKNVLTLVVLVRGIFFFQAYSFPNDYSFCWHFSEGILEISLRVRKATNCRQLPVGLTFCRIHAWCAE

GGQGVKNRKHLMCEFISGSRRLPLRWLMLPAVPPMSILQGLSVLWGYEQASEWQDYLENLG

The following DNA sequence Seq-2284 <SEQ ID NO. 8> was identified in *H. sapiens*:

TTAAAAACAAGTGGTAATTAAATTTAGCTGGCAAGCTAAAGTTTGTCAATTCTTGGTCTAGAAGAAGAAAC
AGACACAAGCCAAAAAATTATGCATATGATAACACGTGCAAAGATCCGGTGGCGAGAAGACATATCAAGCT
TTGGAGGCACTGATAGGAGACCAATGGAGCTGCTTCACGGAGAGACACATGAGTGAGGCTGGAAAGGGAGG
AAGGGGCAGGCCAGCAGGGTCTTGTAGGACACTTAGGAGTTTGGTCTTTACAATATTGACAGTTGGCAATT
TTTTGATTATTTTAAGCAGGATGAAGACATGATCAGATTTGAGTTTCAAAAGCTCACTCACTGCAGTGTTA
GAATGAGTTGGGTTAAATTTTCTCATCTGAAACATAAGGATGGATACACTTGCCCTGTGTATTGAACAGGT
CATTGTGTAATCAGTGATCACACAAGATTTATACAAGGTGCATAGAAGTGTTTTATGAAATATAAATGCTA
TAGAAAATTACACAGCAATATTTTACAGGAAGCAATACCACCAGATGGTCATATTCTTTCAAGTTTTTTCT
GTGAACAAAGGCAGTCTGAACTCATAAAAT

The following amino acid sequence <SEQ ID NO. 136> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 8:

ILVQTAFVHRKNLKEYDHLVVLLPVKYCCVIFYSIYISNTSMHLVILCDHLHNDLFNTQGKCIHPYVSDEK
IPNSFHCSEAFETQISCLHPANNQKIANCQYCKDQTPKCPTRPCWPAPSSLSSLTHVSLREAAPLVSYQCL
QSLICLLATGSLHVLSYAFFGLCLFLLLDQELTNFSLPAKFNYHLFL

The following DNA sequence Seq-2285 <SEQ ID NO. 9> was identified in *H. sapiens*:

CTAAACTCTCTGTAGAGAGCATGCAGTGACAGTTTAGCCTATGCTACCTGAAGTGGAAATAGATCATTCTT
TAAATAAATCACTTGTGCTGACTTGGTAACTCAAGGAGACCACACTTATTATTTCCTCTCAATTCGCAACT
ATCTTTGGAAACAAGACGATTTTATTTCTTGCTTAGCCTTACCTCTTCTATTCACAGAAAATCAGCAGCAC
GCTAATGATGTCTTAAAAGTACAAAGTCACTTGTAAAGGACATTAGGATCCCTGGCTAGGTAAGAAACTCT
GTATGACACAGTTTTCAAGTGCACACCTATTCAAAATTGCAAGTGATATCTCTTTTGTACTGATTTAGCCT
GTACCTGAAAGCAATAGCCATACACATGAGTATACTGAATTAAGTGCACTAGTAGATGACTTTCTATAAGA
AAGAGGGGGAAACACCCAAATTACATTCAAAGACATTACTGGAAATTAATTATGTATAATTCCCAGTATAA
TGCAAACATTTATCCTCGCGTTATCCAGTTTCTAACTGTAGGAGAAATTGCATTTATTCCTTAAAATTTAA
CACTACTACGCTTAAAACAAAAAGTCATGCTAGTATGCATATTTCCACAAATCTTATAAAATAGATGATAT
TTTCA

The following amino acid sequence <SEQ ID NO. 137> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 9:

LNSLRACSDSLAYATSGNRSFFKITCADLVTQGDHTYYFLSIRNYLWKQDDFISCLALPLLFTENQQHAND
VLKVQSHLRTLGSLARETLYDTVFKCTPIQNCKYLFCTDLACTKQPYTVYIKCTSRLSIRKRGKHPNYIQR
HYWKLIMYNSQYNANIYPRVIQFLTVGEIAFIPNLTLLRLKQKVMLVCIFPQILN RYF

The following DNA sequence Seq-2286 <SEQ ID NO. 10> was identified in *H. sapiens*:

CTGGAAAGGAAAAATCTGACTATTTCTCCACTACAGCCATTTTCTAAAAGCTTCTGGAGGCTGTGTGCATC
CCTTCTAGTGAAGTATCTGGGAGTTCACCCTGTGTTGCAGAGAGAAGACTCCACCCCTCCTCCCTCCCCAA
AGCTACCACAGCTTACTTGAGAATAACAACAATATCATGTGACCCTTACATAGCAATGGTCAATTTATCCA
TTGATCTCTACTATATAATGGGATTGTGACAGCAATTTTGTAAGTTGGATGAGGATTAATTTTATAAATGA
GAATACTGGAGGCTCGGAGAGGTCACCTGTGATGGTCACATACCTGGCTCCATGTACACTATTTCCCTCCT
GGGCCTTTGCCATACTGTGCTGAGCTGCAGTTGGGGAAATATCTCAGGGACGTGCCTCATCAGGGTAGTCT
GTTGTGGACAGCAGAGAGATGGGTGCGTCTCTGGCCACTTATAGCCACACACACAAGTGCCACTCAGAACA
CTGGCCCTGACCCTAAAGAATCAATTAGTGGTCTGCCTGCAGCGAAACTGTTTTCAAGGCCCTTTTAGTGC
TCTCACATTCCACCAGGTATCCCCCTTGGCCCCATGAGCTTGACAGTCTTCCAAAATATTTCTGACAACCC
CAGTGAGTGATGTTCACCAGATGCTGATC

The following amino acid sequence <SEQ ID NO. 138> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 10:

GKEKSDYFSTTAIFKLLEAVCIPSSEVSGSSPCVAERRLHPSSLPKATTAYLRITTISCDPYIAMVNLSID
LYYIMGLQQFCKLDEDFYKEYWRLGEVTCDGHIPGSMYTISLLGLCHTVLSCSWGNISGTCLIRVVCCGQQ
RDGCVSGHLPHTQVPLRTLALTLKNQLVVCLQRNCFQGPFSALTFHQVSPLAPAQSSKIFLTTPVSDVHQM
LI

The following DNA sequence Seq-2469 <SEQ ID NO. 11> was identified in *H. sapiens*:

GGGGTTGGAAAGATCACTCTGACACTGTGGCGGGGGCCTGCTGGGAGCAGGAGTGGAAGCAGGGATGGGAC
TTTTCTCTGCAGCCTACCTAGATCATGGTACTCACAAGCCTTGTTCTCGCAGGCCTCACCTGCTTTTCAGC
CCGGGGCGCCCTGGGCAACCAGAGTGCAGAGGACACGTGTTCATCAGTCTTCACCCCGTACTGGCAACTTT
CTTGGTGCAATGCCCTTGACTGGGCACTGGGAAGGCTGTAAAATCAGTCTTCACCCCGTACTGGGAACTTT
CTTGGTGCAATGCCCTTGACTGGGCACTGGGAAGGCTGTAAAAACAGTTTCTGCCCCCAAGAGGAGCAAAG
GGTGGGCTTGCACCCAGATAACTGCCCCACAAATGGCATGTGCTGAAGACCTGGGGGCGCAGGTGCTGTGG
CCCTCATGCTTTTCCCCGTGCTCCTGGAAGGAGGCTCAATGCCTTGGCGCCAGCTTCATGGTTCTTGGGGC
TCCTG

The following amino acid sequence <SEQ ID NO. 139> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 11:

GWKDHSDTVAGACWEQEWKQGWDFSLQPTIMVLTSLVLAGLTCFSARGALGNQSAEDTCSSVFTPYWQLSW
CNALDWALGRLNQSSPRTGNFLGAMPLTGHWEGCKNSFCPQEEQRVGLHPDNCPTNGMCRPGGAGAVALML
FPVLLEGGSMPWRQLHGSWGS

The following DNA sequence Seq-2470 SEQ ID NO. 12> was identified in *H. sapiens*:

CAATAATGATCTAGGACAGAGATGTTCAACCCTTTGGGGATCTCAGGGCCCAGCCAGGGGAGCAGGGGTGA
GTGTCGGAAGTCTTGCTGTCCACAGCCATCCTCAACTCCCCAAACCTGCAACCAGGGCCGCTCAGCTTTCA
TGAGCTTACCTCCCAGCCTCTTTTTTAGTGCTGCCTTTGGAGAAAGAATGACGTGGTCAAAACCTTTGAAA
ATCAGGATTTAAACAATAAATTTTAAATATAAGCAAGATGCTTTCCTATAGGAAAAAAAGAATACATGAAC
GAAATTCAGCTTTCTACATCTGCAAATTCAACTGATAGTGAATTTAAAGGGCCATTTCCTGCCCTGTAATG
ATCACTGATGACATTGACAGGCTGCTTCTCTCTTTCTTGGCTGCACCTCATGGGGGCATCCTGGCACCTGC
TTTGTGGTCAGGGTGTAGAGAAGACCCCCCCAGCTGTCAACTCTTTAACTGTCAACATCTGCGTCAACATC
TGCTTAGAGGATCTTAGTCACACACCAACAATTCTTACTTAAAATATAAAGGGCCACGGGGATGAGTCTTT
GAACTCTGCGCCCTCCCTTCCCTTGCAAGGCCAAATGTGTA

The following amino acid sequence <SEQ ID NO. 140> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 12:

IMIDRDVQPFGDLRAQPGEQGVSEVLLSTAILNSPNLQPGPLSFHELTSQPLFCCLWRKNDVVKTFENQDL
NNKFIARCFPIGKKEYMNEIQLSTSANSTDSEFKGPFPALSLMTLTGCFSLSWLHLMGASWHLLCGQGVEK
TPPAVNSLTVNICVNICLEDLSHTPTILTNIKGHGDESLNSAPSLPLQGQMC

The following DNA sequence Seq-2471 <SEQ ID NO. 13> was identified in *H. sapiens*:

TACCCTCCCCTTCTGCCCTCCTAACGAGAACTGTGAGTTGGATGCAGAAGTTTCTAAAAAAAAAAATTGAG
TATTGAAATTGGCTGTTGCATCAGTGAAGAAAAGCAACATCCCTACCACCCCTCAAAAGAGACATTAAAGT
AGTTGGATTAAGGGCACGGGAGTATTTGCTTTCCGATTTAGTGATAATGTGAGTGCTTAATGAAATGACTA
ACACATTCCCTGATTATAGAGCTGGTCAGTGGATCTTGCTGAGTTTCCTGTGGACCTATGTGAAATGATCG
GCATCTGTTCAGGGTTTACTAGGTGCTAAGCACCTTTACATGTGACATCCATTGAATGCTCACAACACCCC
CAGGAAATTGGTACCAGTGTTATCCTCATGGTACAGTGAAGGATACTGAGACTTAGGTTGCATAGCCTGCA
GGTTGGACACACTTCTTTCTGACTGCTGGGGAGCTGTGCTTTTAACCACTGCTGATCCGGCTTGTTTTCCC
CAGATGCAGGCCTGGGGTAGTCTCCTTTCTGGACTGAGAAGAGAAGAATGGAGAAGCCCCTCTTCCCATTG
TGAGTAGACAGTAAATGGTTAGAGAGTAGCCAGGAGCTTCTGGAAACCAGAGTTCCTTTCCTCAGCTGAAA
AGAACCCTAAGAGTAGACTGCCTGGGATGGCGTGCGGGATGGGAGGATCACTGGACCTGTGGGCCAGAAAC
TTGGGTTTGAGTCCCAGCTCTAGCTTTGCTTAGTTGTGTGACTCTCAGAAAGTCATCCAACCTCTGTGGT
GCTTATTTTCAGTGATAGTACCTGTGGGCACATAGGACCTGTGGGGAATGATTACCTTTTAGCCCCATCCT
ATGACAATATGGTTTGTTTTTAAATCCAGGTTAGCACTGACTTCTCACTGACTTCTCTTGTGTTTTCAGAG
TGCCTTTGCATTGGTTTGGCTTTGGCTACACAGCACTGGTTGTTTCTGGTGGGATCGTTGGCTATGTAAAA
ACAGGTA

The following amino acid sequence <SEQ ID NO. 141> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 13:

YLFLHSQRSHQKQPVLCSQSQTNAKALKHKRSQEVSANLDLKTNHIVIGWGKVIIPHRSYVPTGTITENKH
HRGWMTFESHNAKLELGLKPKFLAHRSSDPPIPHAIPGSLLLGFFSAEERNSGFQKLLATLPFTVYSQWEE

GLLHSSLLSPERRLPQACIWGKQAGSAVVKSTAPQQSERSVSNLQAMQPKSQYPSLYHEDNTGTNFLGVLA
FNGCHMRCLAPSKPTDADHFTVHRKLSKIHPALSGNVLVISLSTHIITKSESKYSRALNPTTLMSLLRGGR
DVAFLHCNSQFQYSIFFFRNFCIQLTVLVRRAEGEG

The following DNA sequence Seq-2472 <SEQ ID NO. 14> was identified in *H. sapiens*:

ATTAGGAGATTTATTTTAAGGAATTGGCTCACATGAATGTGGGGGCTGGCTAAGCAATCTGAAATCTGTGA
AGCTGAAACTCAACAGGTATGGGCCAAAGCTTTTATCCACAGACAGACTATCTTTTCTTTTTGGGACAAGC
TTCAGCCCTGCTTTTTGAGTCTTCCCACTGATTGAATCAGTCCTACCCATAATATACAAACATAAATCCTG
AATTTTTTTTAGACTTACCAAATTCAACTGGTTGTGGACTGAATTACATCTGCAAAAGGTCATCACAGAAA
CAGCTGGATTATCATTTGATTGAGTAACTGGGGGCTATAGCCTAGCCAAGTTAACATATCAAAGTCACTGC
AGATGGGTGAGTTGAATAAAATCTTTACCAAAGATGATGCTTAGAATGCATTCCAACAAAAGTTTTAATAT
TTAATGACAGAAAAGGAAATATTATACATACCTAAAAGCTTCCTCCCTACTGTATTAAACTCTCCACCAAA
GGATTTTCTGAAGGAAACACTTGAAGGTATTGATGACAACTGTATAAATAAAAGAGTTATTCTGATTATTA
TTGAGAGATATAATGCTCATTTTATTTATTACATTTGGAGAGCTCTAAATAAGTTTGTAATTATGGCCTGT
AAAAGAAAAAAGTGTTAATTTCCTTTTAAATGGACAACTAAGATTTTTTTATAATATTGAACTCATTAGGC
CAAAACATGCATTCATTTTGGGATTATTTAAATGAATTAATTCATTCAACAGATATATAATTGAAACATAG
TATACAGAAGACATTGTGCTAGATTCTGGCGATAAAATGGTGAATAAAACCAAGACTGCCCCTCCCTTCAA
GAATTTTATGATTTAGTCATGGAAAAAATACATTAATCAAATATTGACACGAAAAAATTATCACAAACTGC
GATAATTCGTGATAGTATAGTTGCAATGAGTCTATGTTCAATGATTCTTGATTTTTTCTGTGTGTTAGAAA
GCTTAC

The following amino acid sequence <SEQ ID NO. 142> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 14:

KLSNTQKKSRIIEHRLIATILSRIIAVCDNFFVSIFDCIFSMTKSNSREGQSWFYSPFYRQNLAQCLLYTM
FQLYICMNFIIIPKMHVLAVQYYKKILVVHLKGNHFFLLQAIITNLFRALQMIKALYLSIIIRITLLFIQL
SSIPSSVSFRKSFGGEFNTVGRKLLGMYNISFSVIKYNFCWNAFASSLVKILFNSPICSDFDMLTWLGYSP
QLLNQMIIQLFLPFADVIQSTTSIWVKKFRIYVCILWVGLIQSVGRLKKQGSLSQKEKIVCLWIKALAHTC
VSASQISDCLASPHIHVSQFLKINLL

The following DNA sequence Seq-2473 <SEQ ID NO. 15> was identified in *H. sapiens*:

CTCTTTGAGGCATATAATGCTCATTCCATTTTTCATACTGCTTAACCTCTCTTTTATATTTTCTATAACTC
TCTTTCTTCACTTTCCAGAGTTCACTAATTCATTCTTTGGCTGGGTTTAATCTAGCTTTACCTTATTCACT
GAGTTTTTTAAATAAATATTTGAATTTCTATGTGACATTTAAACATTTCCTATGTAATTTGCTGTAACTAA
CTTGACATACTGAAATTTTACTTAAAGTGTTATCTTGCTACATCCTCAAATGAGTATCAGTATGTTCACTC
TTTTTTCCTAGAGATAACTGTTTCTTTTGAACTTTCTACATTTCTTTTTTTCTATGTTTTCAATTTTTCCA
ACTCTATTACAAAAAATTTCAGACAGAAAATCTGAACAAATGGTACAATTAACATCGAAATTTTCTTAGAT
TCTAAGATTATCTTTTCGTATTTGCTTTTCTCTTTCTCTGCATGTTGATTTCCATCACACCATTTGAAGTT
AAGTTTCCAAGTAACTGACAGAGATAGAAATGAAATAGTGGTTATTTTTAGTGAATTGGGAGGGGCACAGG
AGAACCCTCTAAAGCATCAGGAAATGTCCTACATCTTAATCTACATGGTAGTTACACATGTAAAAACTCTG
AGCGATATACTTCAGATTTGTACCCTCTACTGTGTATAAGTTCCATCTCAAAAAAGCGTGGGTTTGCGGGG
GAAGTTGCAGTCATCCTAACACTTTACTCCTAAATACTTATACATGTAATTCCTAAGAACAAGGACATTCT
CCTATATAATTACGTTACCATCCTCACATTTAAGAACGTTAATTCCATAACAATATGTAGTATTCAATCAA
TGTTAAAAATTTCCCAAGTCCCAAGAATGATTCTTCCCCCCTCAGGATTACACACTGCATTTGGTTGTTAT
GTGCACTTGGTCTTGTACAGTGTGGAATAATCCCCAACCTTTTTATTGTCCAAGACATTAACTTATCAAGG
AGTCTA

The following amino acid sequence <SEQ ID NO. 143> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 15:

LGICSFHFSYCLTSLLYFLLSFFTFQSSLIHSLAGFNLALPYSLSFLNKYLNFYVTFKHFLCNLLLTHTEI
LLKVLSCYILKVSVCSLFFPRDNCFFTFYISFFLCFQFFQLYYKKFQTENLNKWYNHRNFLRFDYLFVFAF
LFLCMLISITPFEVKFPSNQRKNSGYFIGRGTGEPSKASGNVLHLNLHGSYTCKNSERYTSDLYPLLCISS
ISKKRGFAGEVAVILTLYSILIHVIPKNKDILLYNYVTILTFKNVNSITICSIQSMLKISQVPRMILPPSG
LHTAFGCYVHLVLYSVESPTFLLSKTLTYQGV

The following DNA sequence Seq-2474 <SEQ ID NO. 16> was identified in *H. sapiens*:

CCAGGCAGAGGAAACTGTAAAGTCAAAGACTAGGGTAGGGGAGGAAGGATAAGCAGAAAAACACTGAGAAT

TTATATACTGGCAAGAAACCCAGGTGACTGGAGCAAAGCAAACCAGCAGCGAGCGGATGGCATGGAGGCTG
GAGAGCCAGGCAGGGGTCAAAGTCCCCGTGCAAGGAGCTTGGCTGTCATTCCATGGGCTACTGGAGAGAGA
AGCCGTGGAGCAATGGGATCCGATGTTAACTTGAAAGAGATCACTCTTACTCACCAGTGAAACTGAGTGAA
CTACTCACATGCTCAGCCATTTAATGGATCTAGAGGGAATTATGCAGAGTGAGAAAAGCCAATCCCAAAAG
GTTATATACAGCATTGATTCCATTTACACGACACTGTTGAAATGACATTGCAGAAATGAAGAACAGATTAG
TGGTTGCTGGTAGTTAAGGAGGGGTAGAAGCATCCGGACGGTGGTTATGAAAAGCCAACACAGGGATCCCT
GTGGTAATAAAGCCGTTCTGTAACTTCCTTGACTTTGTCAATGTCAGTATCCTGGCTATGATCCTGTACCA
TTGTTTTGCAAGATGTTACCACTGGGGGAACTGGTTAAAGGGTATACTCTTCATATTATTTC

The following amino acid sequence <SEQ ID NO. 144> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 16:

EIIRVYPLTSSPSGNILQNNGTGSPGYHQSQGSYRTALLPQGSLCWLFITTVRMLLPLLNYQQPLICSSFL
QCHFNSVVMESMLYITFWDWLFSLCIIPSRSIKWLSMVVHSVSLVSKSDLFQVNIGSHCSTASLSSSPWND
SQAPCTGTLTPAWLSSLHAIRSLLVCFAPVTWVSCQYINSQCFSAYPSSPTLVFDFTVSSAW

The following DNA sequence Seq-2475 <SEQ ID NO. 17> was identified in *H. sapiens*:

ATGATTTTTATTTGAAAAGTCACATTGCACAGAGTGATATATAAATGAATTTTCTGAAGATATATGTGTTA
AATCAGGGCTTTCAGGCACAGTCTGCTTAAAACTTTGGAAAGAGATACTATTTTTTTTCAGTGCATTTGTA
TCTTCTAATTTTCTCATAGTAATATCACAGGGTCCCCATAGGTGATGCTGAATATGGGCAACTGGTTTTTT
TTGTTTTTTTTTTTTTTACCTGTTGTCTTAGCATTCCCTAAAACAGGGGTCACCAAATCCCAGGCCACCTAG
TGGTTCTGGTCCATGGCCTGTTAGGAACGA

The following amino acid sequence <SEQ ID NO. 145> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 17:

FLFEKSHCTEYINEFSEDICVKSGLSGTVCLKLWKEILFFFSAFVSSNFLIVISQGPHRCIWATGFFCFFF
FTCCLSIPNRGHQIPGHLVVLVHGLLGT

The following DNA sequence Seq-2476 <SEQ ID NO. 18> was identified in *H. sapiens*:

AAGACTCAAGATACCATGAATTAATCCAAGTCTCAGAAAATAATTAAAAAAAAAAAAAGACAATCCCGATGA
GGTTACAGGACACAAAAGATAACATGAGTCATCACCGAATAAGACTAGGAGGCCTTCCGGAAAGGGACAAT
TGGGGGAAAAGCTTGCCAAAACTCTTCATTAAACACAGT

The following amino acid sequence <SEQ ID NO. 146> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 18:

TVFNEEFWQAFPPIVPFRKASSYSVMTHVIFCVLPHRDCLFFFLFSETWINSWYLES

The following DNA sequence Seq-2477 <SEQ ID NO. 19> was identified in *H. sapiens*:

TTGTCTGCTTTGTGATCATCAGCTTCTTCCTTTGGGTCCTGCCCTTAGTTGTCCTTGTGTGCCTGCCAGGA
AAGTTTCTGACCCTTGCCTTTGACCTCCTGTTGCTACTGTCCATTGTGGTCAGCATGCCTCACCTAGTCAT
CTACTTCTTGGCTGAGTAACTCTACAGGAAGAGGCACAGGGAGTCCCTAAAGGCTGTTTTTCAGAGGGCTT
TGTTGAGTGAGATGGAGGCATGGATAAAATGAGGCGTTTCAGGCCCCCGATCCCAGGGCAGATTTCAGCCT
CACAGCTGGAAACAAACTGCTCTTCTAGGGGGCTCAGCTCCTCCACAAAGGCAGGGACTGCCTATGCACAA
GGCTGTAAAAGGGATCATGTCTGGAAAACATGCTGAATCCTCCAAGGAGCAGGGTGAATGTTCTTGAGATT
ATTTATTACCTTTGTGTATTTTCAGAGTAACCAGATTTCTGACTGAATTCAAGACAAAATTACTTTGCTTC
TGTTGATAGCCCATTATTCTCAATTCCCATGGAAACCCTCTGGAAAGGCAGGTCAGGAGCAAAGCAGACCT
TCCTGGCTTCTTCTTTTTTTTTTTTT

The following amino acid sequence <SEQ ID NO. 147> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 19:

VCFVIISFFLWVLPLVVLVCLPGKFLTLAFDLLLLLSIVVSMPHLVIYFLAELYRKRHRESLKAVFQRALL
SEMEAWIKGVSGPRSQGRFQPHSWKQTALLGGSAPPQRQGLPMHKAVKGIMSGKHAESSKEQGECSDYLLP
LCIFRVTRFLTEFKTKLLCFCPIILNSHGNPLERQVRSKADLPGFFFFFF

The following DNA sequence Seq-2478 <SEQ ID NO. 20> was identified in

H. sapiens:

CACGGCTAATAATTACAACACAGTGTTTCTGCTTTCTGGACAGCACAAAATACAGCTTTCAGCTGTTTTTA
TGTAGGCCACATTCTCATACCTCCCTTCCCAACACAGAGAACAGTATAACAGAATACTGGGAACACAATTA
GGAAATGAAATTAGAAAAAGGGAGCATCAGGTAAAGCAAGCATTTAAAGAAGCCAAAAAGGCTTTCTCCTA
ACAAGAGGCACAAACGCGTGTGAGCGGCCGGCGAGTCCGAGCTGCACTGCGGGGCCGCTACCTTCAGACTT
CCCTGTACGCTCCACACTTCCACAACGGGCGAGGCTACTTTTATAATCATAAAAAATGCCCAATCAATACA
ATTTTCAAAAGAAGAAGCGGAAGGGAAAAACCAATC

The following amino acid sequence <SEQ ID NO. 148> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 20:

IGFSLPLLLLKIVLIGHFLLKPRPLWKCGAYREVRRPRSAARTRRPLTRVCASCEKAFLASLNACFTCSLF
LISFPNCVPSILLYCSLCWEGRYENVAYIKTAESCILCCPESRNTVLLLAV

The following DNA sequence Seq-2479 <SEQ ID NO. 21> was identified in *H. sapiens*:

CTTTGACATTTTGTTATAAGCTGTAACCTATATGTCTCCTTATAAATAACATTTCTTGACTGCCAGCTTTA
CTGATCGAGGATTGGATTATATTTTAAACATATCATGGCGTTGGTTCCAAAACAATGGTCAAAGCAGCTTG
CCAAAAAAAAAAATACCAAGAGGGATATATCCTGATTGATTCTCACATTCCTCTCAGATACATTGGTAAATG
TGATATACTGGTCCTATAAATGTACTGAACAACGTGTGACAGAAACCAGGCAGGGACATTCCTGAAGGCAG
GTTGCCGCAGCTGTCTATAGCCACATACCTGATATGCAACAATCTGCATTCATTCTGATTGTATCAGGTGA
AAGCTATG

The following amino acid sequence <SEQ ID NO. 149> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 21:

LSPDTIRMNADCCISGMWLTAAATCLQECPCLVSVTRCSVHLDQYITFTNVSERNVRINQDISLLVFFFWQ
AALTIVLEPTPYVNIIQSSISKAGSQEMLFIRRHIGYSLQNVK

The following DNA sequence Seq-2480 <SEQ ID NO. 22> was identified in *H. sapiens*:

ACTAGATGGTTCCCATGTCGCCATTAAGGTAGTGCAGGTTAAATCCACACACAACACTAGGTGTGGTTGTT
CATGCTTTCCCATACTCATCAGGAGATCAGAATTGTATAGGTCCTGTCCGAAGAGGTACCTGGATTTTGGA
GTCAAACAAACCTTGATTCTCTCATTTCCTAGTTGGGTGACCTTGAGCAAGTAAGTTAACCTTTCTGAGTC
TCAGCTCATCTATAAAATGGGAAAAACTACACCTACTTCATGGGACTGCAATTAGGTTTAAGATAATGGTT
ATCAACAACCTAGTCCAATATTTAGTATATACTAAGTGCTCAATAAATGCTACTGCTATTTGCTCCTCTCA
TCCTATTCTTTTCTTTGTGGATAATCGGTTCAATTCTCTCAGCATCAAACCAGGTAAGAAAAGGGATGAGC
ATCGACCGTGGAGCCGGTCAATAAAAGACAGCAAAGGCTTCTCCTCTGGCCACCCCTTCCCCATGTGTTGG
CCCAATCATGTCCCACTTTGGTCCTCAAGGTTATAGTATGGGCTGTTCAATTCCACAAAGGCCCAAGTTAA
TATCTGACCAACCCCAAGTAATTAAATGAGTACTGGCCCTGTTGGCAACTCTGTTGCTGGACAGGCCTTGT
GTTCAGTTTCAGCGCATGGACTGAGCACGCACCCTGATCAGCCCCCCGTGCTCACTGCTTTCTTACATCAA
ATCCTCACAAGCAACCACCCG

The following amino acid sequence <SEQ ID NO. 150> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO.22:

MVPMSPLRCRLNPHTTLGVVVHAFPYSSGDQNCIGPVRRGTWILESNKPFSHFLVGPASKLTFLSLSSSIK
WEKLHLLHGTAIRFKIMVINNLVQYLVYTKCSINATAICSSHPILFFVDNRFNSLSIKPGKKRDEHRPWSR
SIKDSKGFSSGHPFPMCWPNHVPLWSSRLYGLFNSTKAQVNIPTPSNMSTGPVGNSVAGQALCSVSAHGLS
THPDQPPVLTAFLHQILTSNHP

The following DNA sequence Seq-2481 SEQ ID NO. 23> was identified in *H. sapiens*:

TCATTAAATCTCTTATTTACTAGTCTAACTCTTCAGCCCCAAGACTGTCTTGAGGAGTTCGAGTACCACGG
CATGGCCAAGAGGCCAGCCCAGCAATGATATCTGTCTTCTAAGCTTTGATTTCCAGCCTTATCTGAGAAGT
TGAAGTGGGGGGTAGGGGACACTCCTGCTGCCAACTGCCCGCACTCACCAGTGATGAGGTTGTCCAAAGGG
TTGGTGGGCATGCAGAAGATGCCCACCAGCAGGTCACTGACAGCCAGGTTGAGGATGAACATGTTGGTGAC
AGTATGCATGTGCCGGTTCTTGAGCACGATGAAACAGACCAGGGTGTTGCCCACCATGCAGAGCAGGAAGA
TGAGCGCATAGGCCACAATGAACATGGCCGCCACAGGGGAGGTGTGCTGATAGTAGGAGGAGAAGGTGAGG
TTTGTAGCCGGGGTGGCCTCAGTGTTAGTCCCATTCTGACTTAGGGGCCAACTGCTGTTGGGAGGCTGGGA

GGGCTCCCCTAGGACCAAAGGAATATATTGGTCAGGACCTTAAGCAAAGAAGAGATTACCGATTTCTCACC
ACTAATGAGACCCTCTGTGTGCCAAACCTTAACCATGCCCTGGTCCCCCAAGCATG

The following amino acid sequence <SEQ ID NO. 151> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 23:

MLGGPGHGGLAHRGSHWEIGNLFFAGPDQYIPLVLGEPSQPPNSSWPLSQNGTNTEATPATNLTFSSYYQH
TSPVAAMFIVAYALIFLLCMVGNTLVCFIVLKNRHMHTVTNMFILNLAVSDLLVGIFCMPTNPLDNLITGE
CGQLAAGVSPTPHFNFSDKAGNQSLEDRYHCWAGLLAMPWYSNSSRQSWGRVRLVNKRFN

The following DNA sequence Seq-2482 <SEQ ID NO. 24> was identified in *H. sapiens*:

ATGCTTCATTTGAAAGTTACCAAACTGTGTGTGCACATACACATTGCAAATCCTCCCAAACTGTAAATGTC
TCTGCTATGGTTTGGATATGGTTTGTTTATCCCCACCAAAATTCACATTGAAATTTCTTCCCCAGTGTAGT
AGTGTTGGGAGGTGGGACCTAGTTGGGGAATGGCTTGGTGCCACTCTCTAGGTAGTGGCTGAGTTCTTGCT
GTGGCGAGAATGAATTAGTTCTTGCGGGAATGAATTCTTAATAGTTCCTGCCAGAGTGAGTTTTTATAAAG
CCAGGATGCCCCTTGGGTTTTGTCTCTTTTCACATGTCCACTTTCCCTTTGACCTTCTCTGCTGTGTTTTG
ACCTAGCATGAGACCTTCACCAGAAGCCAAGTAGATGTCAGCACCGTGCTTCTCTAACTTTCCACCTGCAA
AACTGTGAGCTAAATAAACCTCTTTTCTTTATAAATTACCTAGCCTCTGTATTCTGTTATAGCAACACAAA
ATGGACTAAGACGGTCTCCCAAACCAACTGTGGGCTTTTCTTAAAGGTCACCCCGACA

The following amino acid sequence <SEQ ID NO. 152> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 24:

MLHLKVTKLCVHIHIANPPKLMSLLWFGYGLFIPTKIHIEISSPVCWEVGPSWGMAWCHSLGSGVLAVARM
NFLREILNSSCQSEFLSQDAPWVLSLFTCPLSLPSLLCFDLADLHQKPSRCQHRASLTFHLQNCELNKPLF
FINYLASVFCYSNTKWTKTVSQTNCGLFLKVTPT

The following DNA sequence Seq-2483 <SEQ ID NO. 25> was identified in *H. sapiens*:

CTTAATACAGAATGATGTCAGCATGAACCAGAAGTCATGTTGGTTCATGGGAGATTTCTTTCCAATGTTAT
TTTGAGTCACCAAGTAACAGCAGCCATGAGCAAGATACATAAATACAGTGCATGCAAGCCCAAGAGGCCTG
TAGTACTGCATCCCACATGCTTTCTTTTCGTTTGGTTTGGTTACATGTTCTGTCTTGGAATTAACTGTTTA
TTGTACAATCTTCCTGGATCCTTGAGCATTTTGCCCTTGCATCCAAAATTGGGCAGCCTCAACCCTTACAT
CAAGTTTATTTCACCTGTAAACTCTGCTAGCATTTTAATTTTTACTGCTTTTCTGAGTGCTGCGCTTATCA
AGTTCAATATATTTGAAGTGGACTACCCTTTACCTTATTTCCCCCCCACCACAAAAGCCCTGCAACTTTTA
CTGTAGTATTCTGCTGAACACAGGTGGGAACACAGATGTCATATTACAGCAGAAATATCTATTCTTGTGAG
GACACATCCTGACAGTGACATGAAGTGACACATTGTGCATACCACTATAGCACATCGTTTCCACCAGGAAA
TGTCTGCAGACAGTGATGAGGGTCCAACAACTCCAAGCTAAGGGTGGCGGGTGCTAGACAGCTCGCTAAGC
CCCCTGCCAACTCCCTTCCATGTACCTGCTTCACAACACGAAGCTGCTTCACAACAGTGCCAACGAACAAC
TGATCGACCAAGGACAAATCACTGAATTCATCCGTGGAAGCGAAGCTCTGTGTACTACATGTAAAG

The following amino acid sequence <SEQ ID NO. 153> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 25:

LNTECQHEPEVMLVHGRFLSNVILSHQVTAAMSKIHKYSACKPKRPVVLHPTCFLFVWFGYMFCLGINCLL
YNLPGSLSILPLHPKLGSLNPYIKFISPVNSASILIFTAFLSAALIKFNIFEVDYPLPYFPPTTKALQLLL
YSAEHRWEHRCHITAEISILVRTHPDSDMKHIVHTTIAHRFHQEMSADSDEGPTTPSGWRVLDSSLSPLPT
PFHVPASQHEAASQQCQRTTDRPRTNHIHPWKRSSVYYM

The following DNA sequence Seq-2484 <SEQ ID NO. 26> was identified in *H. sapiens*:

GAAAGCTTAGCCCATGATGGTGAGGTAGTTCCCTTTGGTGAAATGTGAACATTAGCCATTTAATAGTTCAT
TTCCTAAAGTCTAAGTATATGGATAAGGTCTATGCCTTTCCCACAGAGGTGTACAGGTAAGGTGTAATCAA
GTTTGCTTACAAAATTTTTTTAAACTATGACCTTGGCAGAGATGTAGTTGTAATAGAAATTATATTCTGGA
ACTGTAAAAGCAACTAAATGTATAATTATTTGGCTGTTCTTCCTGCTCTTTCTCTGACTCTTCCCATATCT
GGATCCTTCTTACTCATTGGATTTCAGGACAAAAAATGCTTTCTCAGAGATGGCTTTTGTGTTCATCTGTT
TAAACGCAGTCCCCTTTCTTAGTCTTGTCATCTTCTAACAAATTACCATGTTTACTCATTGCTATGGTTTG
GATATGGTTTGCTTGTCCCCACCAAATCTTATGTTGAAATAATGATCTCCAGAGTGGTGGTATTGGGAGGT
GGGGCCTAGTGAGAGGTGTTGGCATCATGGGGGCAGATCCCTTGTAAATGGCTTGGTGCCATTCTCATGGG
AGTGAATGAGTTCTTGCTCTTTTGAGACTGGGTTGCTTCTTGAGGGAAAGGGATTAGTCTCCCTCCGAGTG

GGTTGGTATAAA

The following amino acid sequence <SEQ ID NO. 154> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 26:

KLSPWGSSLWNVNISHLIVHFLKSKYMDKVYAFPTEVYRGVIKFAYKIFLNYDLGRDVVVIEIIFWNCKSN
MYNYLAVLPALSLTLPISGSFLLIGFQDKKCFLRDGFCVHLFKRSPLSSCHLLTNYHVYSLLWFGYGLLVP
TKSYVEIMISRVVVLGGGAEVLASWGQIPCKWLGAILMGVNEFLLFDWVASGKGISLPPSGLV

The following DNA sequence Seq-2485 <SEQ ID NO. 27> was identified in *H. sapiens*:

GTTAGTGGGCATTTTTTTTGGAGCTGTGGCTTCAAATGAGTTTCAACATAAACACTACTTTGAATAGTTGA
TAAAAATGGCAGTATGTGGGTTTACATATTGATTTGGTCGTGCTGATAGTCTTATTAAAGCAAGGCTGTAG
AGGCCAGGTCACATTCTTTCCATGACATTTTAATGAGCAGTTTAGGGAGGGTGGTTGGCGTGGTGATTGTA
AGTGGGGACAAGTGGCAAAGATTAACTCAGTATTCATTTTGCCTGACTGCAGAATTTAAATAACCCTTCCA
CTTGTTGCTGGTACTGTCAACACGTGGTAGAAAATATAAATTAGATTGTGCTCTACACAGACTGTATATAA
TAATTTC

The following amino acid sequence <SEQ ID NO. 155> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 27:

VSGHFFWSCGFKVSTTLLIVDKNGSMWVYILIWSCSYSKAVEARSHSFHDILMSSLGRVVGVVIVSGDKWQ
RLTQYSFCLTAEFKPFHLLLVLSTRGRKYKLDCALHRLYIII

The following DNA sequence Seq-2486 <SEQ ID NO. 28> was identified in *H. sapiens*:

GCACCAGTATCTGTGTCTGATGAAGCCTCAGGAAGCTTCCACTCGTGGTGGAAGGTGAAGGGAGCTGGCAT
ATACAGAGAGCACATGGTAGGAGAGAAAGGCAAGGAGAGAGAGGAGATGGTGCCAGGCTCTTTTCAACAAC
CAGTTCTTGCAAGAATTCACTCTCATGAGTATGGCACCAAGACATTCATAAACGATCCACTCCCACAACCC
AAACAGCTCCCACCAGGCCGTACCTCCAATACTAGGTGGGCATCAAATTCCAACATGAAACTTGGTGGGGC
CACACAAACCATATCCGAACCATAGCAAATGTCTTGAAGGTAAGAATTCTCTACCACAAGCTTCTCTGCTG
GGTACATATGTCCTGCCCATAAGCAAATCTTGGGTGAGCACTGGTGACTAACCAGCATCACAGAAAGAAAA
GACAGATACCAGGGCCCTGTTACCAACAGCCTGGCAAATAGATGACCACACTGGATCTCAATTTACAAAAT
GGGGGTAACCAGGTGGCCTAGATAAATCTTGATAGATATACAGAGAGAGGTAAAGTAGTG

The following amino acid sequence <SEQ ID NO. 156> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 28:

LLYLSLYIYQDLSRPPGYPHFVNDPVWSSICQAVGNRALVSVFSFCDAGSPVLTQDLLMGRTYVPSREACG
REFLPSRHLLWFGYGLCGPTKFHVGICPPSIGGTAWWELFGLWEWIVYECLGAILMRVNSCKNWLLKRAWH
HLLSLLAFLSYHVLSVYASSLHLPPRVEASGFIRHRYWC

The following DNA sequence Seq-2487 <SEQ ID NO. 29> was identified in *H. sapiens*:

TTCACCACAATGAAGAAAACAAATCCTCTTATGAACATGATCTCATTAGTTCCCATAATGACACATTATTC
TGACACGAAGCGAGGTCTAAGAAACTTCAATACTCACTCTCTTTACAGATGGGGAAAGTGAGTCAAAATTC
TGGGAAGCAGCAAAGCAATTATCCAAGCTGGAATTAAAGCCTAGCGTTCTAAATGCTCATTTAGTGCTAGT
GCTACCCAAAATGATTCTACATTTTATAAGCAGGTAATAAATAAATAAATATAAGCAGGATCAGCCAGGAT
GAAGTGAAAATAAAAATAATTCCATGGAGTTTTAACAGCTTTTCTGTAACTTTTGACTGCAGCTCTTTGCC
TGAAGTGTAACATACAAAACCAAAAGAGAGTAAAACAGAGCATACTGAAATCTTGACACCTCTCAAAGAAC
TAGATGGTTTACCCTTTTACATAGGAAGCAAATAAAGGAGAAACTGTCAATGACTGATGGGAACACAGTAC
AAAATTTAAGTTAGTGGTTTATTTTTAAAGCTTGTATAATATGGACTACAAAGGGCATTTTTGAGCCATGC
AAAGGTCACCCACACACTAGTCCCTTCAAACTAGCTTTTTC

The following amino acid sequence <SEQ ID NO. 157> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 29:

KKLVRDCVGDLCMAQKCPLSILYKLKTTNLNFVLCSHQSLTVSPLFASYVKGTIFFERCQDFSMLCFTLFW
FCMLHFRQRAAVKSYRKAVKTPWNYFYFHFILADPAYIYLFITCLNVESFWVALALNEHLERALIPAWIIA
LLLPRILTHFPHLREVLKFLRPRFVSECVIMGTNEIMFIRGFVFFIVV

The following DNA sequence Seq-2488 <SEQ ID NO. 30> was identified in *H. sapiens*:

GCACCAGTATCTGTGTCTGATGAAGCCTCAGGGAAGCTTCCACTCGTGGTGGAAGGTGAAGGGAGCTGGCA
TATACAGAGGAGCACATGGTAGGAGAGAAAGGCAAGAGAGAGAGGAGATGGTGCCAGGCTCTTTTCAACAA
CCAGTTCTTGCAAGAATTCACTCTCATGAGTATGGCACCAAGACATTCATAAACGATCCACTCCCACAACC
CAAACAGCTCCCACCAGGCCGTACCTCCAATACTAGGTGGGCATCAAATTCCAACATGAAACTTGGTGGGG
CCACACAAACCATATCCGAACCATAGCAAATGTCTTGAAGGTAAGAATTCTCTACCACAAGCTTCTCTGCT
GGGTACATATGTCCTGCCCATAAGCAAATCTTGGGTGAGCACTGGTGACTAACCAGCATCACAGAAAGAAA
AGACAGATACCAGGGCCCTGTTACCAACAGCCTGGCAAATAGATGACCACACTGGATCTCAATTTACAAAA
TGGGGGTAACCAGGTGGCCTAGATAAATCTTGATAGATATACAGAGAGAGGTAAAGTAGTGAAAGCCCTAT
GAAAAATGTAATTCAATATGAAAACGTATGGTATTATTACTACAATGCTAATAAGCAATTAAATGTTTCTC
AAAAATAGGGAAGACTGGGAAGAAGGGAAGCATTACAAGCTAAGCTGGCT

The following amino acid sequence <SEQ ID NO. 158> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 30:

ASLACNASLLPSLPYFETFNCLLALYHTFSYITFFIGLSLLYLSLYIYQDLSRPPGYPHFVNDPVWSSICQ
AVGNRALVSVFSFCDAGSPVLTQDLLMGRTYVPSREACGREFLPSRHLLWFGYGLCGPTKFHVGICPPSIG
GTAWWELFGLWEWIVYECLGAILMRVNSCKNWLLKRAWHHLLSLLPFSPTMCSSVYASSLHLPPRVEASLR
LHQTQILV

The following DNA sequence Seq-2489 <SEQ ID NO. 31> was identified in *H. sapiens*:

TTGATTCCTGTCTTGTTGGACACAGAAGAGGCTGCCCAGCTGAAGAGAGACATGTCCTCAGCTTTTCTGGT
GAGTGAAGGCCTGTGCTGGAACTTATGACAGCAAATCCCAGCTCTGAAAGTGGATTTCTATATCTTCCTCT
TCAAACTCACCGTCACTCTAGAGAAAGAACTCTTCTTTCCTGTGTTTTATTTATGTCTAAAACATAGGTAA
ACGGTGTATGTATGATGTCTTCTTCTTATTTATTTCCTTTTGTTCTAATTGCAAAAAATCACACATGTTCC
TTGTAAAAAAATCAACCAACCAACCAACCTTGAAAAACTTAAACAATGAACAAAGAGAAAAGAAATTACCT
AACATCAAACATAATGTGTATACATTACAAAAGCTTGAAAAATACAGAAAAACACAAAGGAAAGAAAAAAA
AATCACTTCCACTCAAAATTATTTCTGTTAATTTCAGTATATAGCCAAGCATTTTTCCATGTAT

The following amino acid sequence <SEQ ID NO. 159> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 31:

FLSCWTQKRLPSRETCPQLFWVKACAGTYDSKSQLKWISISSSSNSPSLRKNSSFLCFIYVNIGKRCMYDV
FFLFISFCSNCKKSHMFLVKKSTNQPTLKNLNNEQREKKLPNIKHNVYTLQKLEKYRKTQRKEKKITSTQN
YFCFQYIAKHFSMY

The following DNA sequence Seq-2490 <SEQ ID NO. 32> was identified in *H. sapiens*:

ACTTTGTCAAAAAAGTACAGAGTATGAACCTCACAGGGAAAAGCCCTCTGAAATCGACCTGCTGGTTAGGG
AATGAGAAGGAGGTAGAGCCAGGCAAGGCCACTCCTTCTGGGTACATAGGGAAAGAAATTAAAGCTGCTAC
AACTAGACAGTCAGAAGTTGCTCAGAAGTGGTAGTCCTAAATGTTCTTAAGGGAGCTACTCTGGTTTGGTT
ATGGTTTGTCTGTCCCCACCAAACCTCATGTTGACATTTTCTTCCCAGTGTGGCAGTGTTGAGAGGTGAGG
CCTAGTGGGAGGTGTCTGGGTCATGGAGGTGGATCCCTCATGAACACTTAGTGCTGCTCTCAAGTTAGTGA
GTTCTAGCTTTGGCAAGACTGAATTAGTTCTTGTGGAAATGGAGTAGTTTCCTCGAGAGTGGGCTGACATA
AAGCCACATGCCCTTCACATGTGTCCACTTCCCCTTTGACCTTCTCTACCATGTTCTGGCAGCACAGAAGC
CTCACCAGAAGCTGAGCAGATGCTGGCACCATGGTTCTTATACAGCCTGCAGAACAGTGAGCTAAATAAAT
CTATTTTCTTCATAAATTACTCAGCCTCAGGTATTTTTTTTTTTTTTTTTGAGACAGAGTCTCGC

The following amino acid sequence <SEQ ID NO. 160> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 32:

FVKKVQSMNLTGKSPLKSTCWLGNEKEVEPGKATPSGYIGKEIKAATTRQSEVAQKWSMFLRELLWFGYGL
SVPTKPHVDIFFPVWQCEVRPSGRCLGHGGGSLMNTCCSQVSEFLWQDISSCGNGVVSSRVGHKATCPSHV
STSPLTFSTMFWQHRSLTRSADAGTMVLIQPAEQAKIYFLHKLLSLRYFFFFFLRQSL

The following DNA sequence Seq-2491 SEQ ID NO. 33> was identified in *H. sapiens*:

CCAGTGTGGCTGAGACAGTGGAAGTAGGTGAAGGGTAAAATGAAATGAGGTTTGGGTAGGTAAGGAGTGGT

CTGGTCATGATAGACTTTGGAATCTATTTGAGGTGAAGTTGGAAGTTTTGAAGAATTTTAACCAAGCCAAT
GGATTTTTATTATTTATACTTATTAAAGATTATTTTGACTGCAGTGTGGAGAATAGAGTAGAAAGAAATAG
AGAAGTAAGGAACCTACTGCTATTTCACATGAAAATGATGTATCATTAATGTCTTTTATCTGCATGGGGGC
TATGCAGGGAGAAGTGGCCAAATATAAGATATAAACGGGAGTATACATGCCAGGACTTGTTGATGGATTAC
ATACTAGTGTTAATAGTTAACCTTCAGTTCTTGAATGGGGAACTTTTACTTATGTATGCAGTATTTATACA
TTATTCTAGATGTGTTTGACTACAAATGACAGAAATTTAATTAAAATGCAATTTGATAAAGAATTTACTCA
TAAGTCATATTGTCTCATATGACTGGGAAATCTAAGGGTGAGTTAGGACTTTAGGAAAAGCTGTATCCCAA
GCCTATAGATGACTTCTGAACTTAGTATTAATTT

The following amino acid sequence <SEQ ID NO. 161> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 33:

QCGDSGSRRVKNEVWVGKEWSGHDRLWNLFEVKLEVLKNFNQANGFLLFILIKDYFDCSVENRVERNREVR
NLLLFHMKMMYHCLLSAWGLCREKWPNIRYKREYTCQDLLMDYILVLIVNLQFLNGELLLMYAVFIHYSRC
VLQMTEILKCNLIKNLLISHIVSYDWEIGVRTLGKAVSQAYRLLNLVLI

The following DNA sequence Seq-2492 <SEQ ID NO. 34> was identified in *H. sapiens*:

GGTTGGTAGCTGCCGCCCTGCACACCAGATTGCCTCCACCACAGGGGGTTCCCGACTGCTCCCCCCGCCCA
GTTCAGCAACTATAAGAAACCATGGCTGGCCGAATCAGAGGCCGAAGGGCTTACTGTTCTAAGACTTTTGG
AACTATCTGTTTTATCCCCTACTTTTTCCAACTACATTGTGTATTACTCCTACTGGTGTAAATATTTACCA
AAGAAAATTTTTTCACTTTAATATC

The following amino acid sequence <SEQ ID NO. 162> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 34:

LVAAALHTRLPPPQGVPDCSPRPVQQLETMAGRIRGRRAYCSKTFGTICFIPYFFQLHCVLLLLVIFTKE
NFFTLI

The following DNA sequence Seq-2493 <SEQ ID NO. 35> was identified in *H. sapiens*:

CACTCCAGCCTGGGTGATAGAACGAGACTCTGTATCAAAATAAAAAAAAAAGAAAAAAAAAAAGTTATGCTTG
TAGAAGCCAACTCAAGATTAATTTACATATTTAAAAATATTTTCCTTGGAAATTTAATACACATCCAATAT
CGATTATCTTCTTTAAGTACTTTGTATCTTATTCTTCCTGTCAAGCTTTGCACTATAAAGGTGATGTCATG
CTTTTCTGCCATGCCTCATGCAGGTGGCACCTCCTTCCTCACCCCCACGTCTTTTCCAGGTGAGCCGCGAT
GCGCAAAAGGTTGGGATGCCTGGCACAGGATGCCAGCTAGTCGATGTCTTTAGAATGCCCCTGCTGTCTCT
CCCGGGGCTAAATCCTATTCCACCGTGAGCCTTCCTTGACCAGCAGAGAATAGAAGCGCCTGGTGCATACA
GGCCACCAAAGGTATCTGTTGAACAGACATGCACACGGCTTCTGCCGTGGGC

The following amino acid sequence <SEQ ID NO. 163> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 35:

TPAWVIERDSVSKKKRKKKVMLVEANSRLIYIFKNIFLGNLIHIQYRLSSLSTLYLILPVKLCTIKVMSCF
SAMPHAGGTSFLTPTSFPGEPRCAKGWDAWHRMPASRCLNAPAVSPGAKSYSTVSLPPAENRSAWCIQATK
GICTDMHTASAVG

The following DNA sequence Seq-2494 <SEQ ID NO. 36> was identified in *H. sapiens*:

TATTTTACAGATTATGTTTTGTAATACGAGCATATTTCTGTGGTTCCATCCACTATCCCTAGTCTTCCCCC
AAAGACACGCTGATGAATTAATTTTTCTGCTTGTCATTGTAATTGTTATGTGTTGTAACTAAGAAAATACA
GAGGGCATTAAGAGAACCTATGAGGTAACTTTGACTTCACTTCAGGGTCCTGGAAGGAGGAAGCAACAATC
CTAAGTGAAACTTGGACAAGAAGCACCCAATAGGTAGACAAAGGGATTGAGGGTATGAGTTGTTAGTGAAC
AGAGGGAAAGAAGAGAGTGACTCACAAAAGAAGAACACAATTTTGGAGGCTAATTACAAGTTAGAAATAAA
ATAATGAGTGAGTACAGAGAGATTCACTCCTCATGACTCCTCTCTTGTGTCATCTCTCCTAGGACATTTGT
CATGTCCTCAAACACGATGCTTCAAAAAATGCTGCTGATCTTGATCTCTTTTTCAGTAGTAACTTGGGTGA
TTTTTATAATTTCTCAGAACTTCACAAAGGTAGGAGAAAATCACCTTTGATGCAAATCACACAGGTAAGCC
CTCACCTGTGCGACCAGCCTCAAGTCAGTTCCACTCTATTAGTCCTG

The following amino acid sequence <SEQ ID NO. 164> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 36:

GLIEWNLEAGRTGEGLPVFASKVIFSYLCEVLRNYKNHPSYYKRDQDQQHFLKHRVGHDKCPRRDDTREES
GVNLSVLTHYFISNLLASKIVFFFCESLSSFPLFTNNSYPQSLCLPIGCFLSKFHLGLLLPPSRTLKSQSY
LIGSLNALCIFLVTTHNNYNDKQKNFISVSLGEDGWMEPQKYARITKHNLN

The following DNA sequence Seq-2495 <SEQ ID NO. 37> was identified in *H. sapiens*:

TCTTCTGATAGCTGTCGGGGTAAATACCACTGACTGGCCTCAGAAAATCTACCCAATATGCTTAATTCCTC
TCCTGAGCAGAGGATAGCAACACTTCAAAGATTATCCTAATTTTTTTATTTGCAAAAGTTTATTTGCAGAA
GTTGTTTTTGCAAAAGTTGAAGAGTAGATAATCCCAACTTTCCATATTCATAGTGCTCACAAGTCGATTAA
CAAACCAACTCTTAACTCCTTTTCCAGAAAAATGCTTTGCATTAACAAAAGTGGAGATACTTAGATTGATT
TGCTCCATTAGCTGGATCCATTACATATACTACTTGATATACTGTTCCCTAGTGGTTTGTATATGCCACTA
TAGTGAAATTCAAAAAAAATGTTCCAACCTATATTTG

The following amino acid sequence <SEQ ID NO. 165> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 37:

FLSGIPLTGLRKSTQYAFLSAEDSNTSKIILIFLFAKVYLQKLFLQKLKSRSQLSIFIVLTSRLTNQLLTP
FPEKCFALTKVEILRLICSISWIHYIYYLIYCSLVVCICHYSEIQKKCSNLYL

The following DNA sequence Seq-2496 <SEQ ID NO. 38> was identified in *H. sapiens*:

ATCAATTAGGAATTCACACTCAATCAACACAACCTCAATGATGAGAATGACACTCTAAAGGACAGGAACTT
AAACTAACTTCAAGGGACCAACACCTTTGAACAAAAAGCCACGTTATGAACCAAAAAAAAAAAAAAAAACC
CAAAAGTAAAACGTTTGATAACAGAATGTGGTGCTGGGACATGAGGCAGACAGTAGTAATTTACAGTGTCA
TTTATCGGTTGCCATTTACATGTCGGTTGAGTTTCTAGTATTTTAATCAAATGTTGTTTCAAGTCATCAGC
ACATTAGTCAATCAAGTTTTAGAGTCCTTCATTCCCAGACTCTGCAACACTGTGATCAGTCTCTCCCCATT
TCTGGGCCAGGCAAACTCTTTGTTGATTTCATTGGGGTGGATCCTAAAATCCAATCAGGCCACAAATGATT
TGGACTGCTGCTACTTCTCTCACCTTGCTTCTTATTTCCTTCCTCTTTATGTTCTCTTTCTCATCCTCATT
TTGTTGTTCCTCAAACTTGTCAAAACTATTTCCCCTTTAGGATCTTTACATTGACTAATTCCACTTCCTAG
AATACTCTGTCCCCCAGATATAAACATGGTTTATTATTTCACTTCATTCGAACCTTCCTCAAATGTCACCT
TCTCCATAAAGCCCACAATGCTAGTTATTTTCTATCACTTCTAGCTCTCGGATATGTCCTTTGCCCTTTAC
TGCTT

The following amino acid sequence <SEQ ID NO. 166> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 38:

QLGIHTQSTQPQEHSKGQELKLTSRDQHLTKSHVMNQKKKKKPKSKTFDNRMWCWDMRQTVVIYSVIYRLP
FTCRLSFYFNQMLFQVISTLVNQVLESFIPRLCNTVISLSPFLGQANSLLISLGWILKSNQATNDLDCCYF
SHLASYFLPLYVLFLILILLFLKLVKTISPLGSLHLIPLPRILCPPDINMVYYFTSFEPSSNVTFSIKPTM
LVIFYHFLSDMSFALYC

The following DNA sequence Seq-2497 <SEQ ID NO. 39> was identified in *H. sapiens*:

AGCTCTAAATGCATAAAGGCCAGGAATTAAGCTGTGAAATTAACCCCCCCAAATTACAAATAATAAAATCT
CACATAGGTGCACGGCCCCAGCAAGCTGAGGGAAAACCCAAGTGCCTGCTGTGCCTTTTTATTACTTGAGG
TATATGGAGTCTCTAATTTAAGGCTAAATATAAAATAAAGCATACACAGCTGGACTTTCAAGTATTTTCAA
AACACATTTAATACCTTCCCGTGAAACGCCCAGAATCTGAGCAGGCATCACTTCGCACCAGTATAAACAGG
AGTTGGCGTGGACCGAACGTACGGGCTTCAAAAGCATATTTAAGAGGGTTGAACAGGAACCTGCAAGCCAG
AGGCCTGAAGGGATCGCAATGCTGACCTGAGCTCACAGTCACACAGTGTCCTTTGCCACACCAGGGCTATA
ATAGAAACCAGCAAAGCTGGTTGACACGGCCAACACCAACAGGGTCTGCCTCTGACCGCAGCTTTGCCTGC
CCCCCACGTACTTTTCGGCTCTGTTCCTCCACTCCAGGGCCAATGGAAAATGAGAAATATCCAAGTCCTCC
TGGCAGCCATGAATGGATTCTCTGTTAT

The following amino acid sequence <SEQ ID NO. 167> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 39:

ITENPFMAARRTWIFLIFHWPWSGGTEPKSTWGAGKAAVRGRPCWCWPCQPALLVSIIALVWQRTLCDCEL
RSALRSLQASGLQVPVQPSICFSPYVRSTPTPVYTGAKCLLRFWAFHGKVLNVFKYLKVQLCMLYFIFSLK
LETPYTSSNKKAQQALGFSLSLLGPCTYVRFYYLFGGVNFTAFLAFMHLE

The following DNA sequence Seq-2498 <SEQ ID NO. 40> was identified in

H. sapiens:

ATATACATTTTATATTACAAATATAGGTTGGAACATTTTTTTTGAATTTCACTATAGTGGCATATACAAAC
CACTAGGGAACAGTATATCAAGTAGTATATGTAATGGATCCAGCTAATGGAGCAAATCAATCTAAGTATCT
CCACTTTTGTTAATGCAAAGCATTTTTCTGGAAAAGGAGTTAAGAGTTGGTTTGTTAATCGACTTGTGAGC
ACTATGAATATGGAAAGTTGGGATTATCTACTCTTCAACTTTTGCAAAAACAACTTCTGCAAATAAACTTT
TGCAAATAAAAAAATTAGGATAATCTTTGAAGTGTTGCTATCCTCTGCTCAGGAGAGGAATTAAGCATATT
GGGTAGATTCTCTGAGGCCAGTCAGTGGTATTTACCCCTGACAGCTATCAGAAGAAAGATGTGAAACCTTC
CTCCGTTCCAAACATTGTGGGATCTTTGTTGCCCCTTTTGAACCAATATTATTCTTTCCACTTTGAAG

The following amino acid sequence <SEQ ID NO. 168> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 40:

LQSGKNNIGSKGATKIPQCLERRKVSHLSSDSCQGIPLTGLRESTQYAFLSAEDSNTSKIILIFLFAKVYL
QKLFLQKLKSRSQLSIFIVLTSRLTNQLLTPFPEKCFALTKVEILRLICSISWIHYIYYLIYCSLVVCICH
YSEIQKKCSNLYLYKMY

The following DNA sequence Seq-2499 <SEQ ID NO. 41> was identified in *H. sapiens*:

ATGGACAGGGGATCTAACCCCCAACCTTGCTCAAATTGCTGCCACTTTTGCTGGGAAGCCCAGGTATCTAA
ATTGCCCAGGGCTCCATATGAGTGGCTGCTCTGCTAATATTCCATGTAGCTCTGCATGTCAGACTGTAGAC
TGGGCTCTCCAGTCACCCTAGCCAGTGTTTTCTGGGTTGCAGTGGTTCCCAGCCTCCCTGGGATGGAGGTC
CCTGTGGGAGGGATGGGCCACCATCTTTGCTGTTACACAGCCTTAGCCATTGTTGCCTTTGAGCTCTAGGG
ATTCTGAGGTGACTAGGGACTGGAAAAGTCCCCCAGAACAGTGCAGCTGCTCTATGGATAAACAGCCAGAC
TGCATTTTCACATGGGTCCGAGGTCCTAGTTCTCTTCCCCAGGCAGAATTTCCTGACCACAGTCTATGACC
ACCCCCACCAGTGTTTTCTGGTCAGCAGCAGTTTCCAACCTCCCTGGGATGGGGCTACCAGAGGGAGAGGT
AGGCCACCATCTTTGCTGTTTCTCAACTTAAGCATGGTGGCCTTT

The following amino acid sequence <SEQ ID NO. 169> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 41:

RPPCLSETAKMVAYLSLWPHPREVGNCCPENTGGGGHRLWSGNSAWGRELGPRTHVKMQSGCLSIEQLHCS
GGLFQSLVTSESLELKGNNGGCVTAKMVAHPSHRDLHPREAGNHCNPENTGGDWRAQSTVHAELHGILAEQ
PLIWSPGQFRYLGFPAKVAAIARLGVRSPVH

The following DNA sequence Seq-2500 <SEQ ID NO. 42> was identified in *H. sapiens*:

TTTCCCTTGCAGTACCACGTCCTGTCTGAACATCCTCTTCTTCTCAAAAGTCATCATGACCTTATTGTCTG
GGACATATTTGGCCTTGCTCTGTTTTGTTCTTTCGTTACTTTTCATACTGTGCTTTCCAAAACACATCAGT
CATCTTCTCTTCACTGGTTGCATGGATGCTGGAGTCTGTGTGGCCTGTGGCAGACAACCCTGTCCATCCCC
CCACTTCCTGGCTAGCAGAACTCTGATTTTGTTAGGGATAGCAGAGTACCTGGCTAAAAGCTTGATTTCCT
AGGGTCTTTTGGAGTTAAGGTGGCCAAAAAACTAAGTCCTGGCCAATGTTTTGTAAGCAGACATCTATGGG
CGGGTCTTCTAGAAACGCTGTTGTTTTTCTGGTAAAGCGGCCGTGTTCTTTTCATCCCTCATGTTTCTCTC
TTCTGGTTTGGAAAGCGGACTACACTTGCTGCCTTCCAAAAGGCAGAAGGAGCTTTGATCTTGAAGTCATT
GCAGACTTGCTGTTCCATGGGAAGAACAGACCTCTACTGGGTTAAGCCATTGTGGTTGGCTGTGTTACATG
CAGCCAAATATGATTATTGATACGTGAGGTGCTTCTCTGAACTCATACTGATATGAGCCAAGCAATTTAAA
CATGTTTAATGGGGCCTTTAAAATGGCATCCGGGCTGGGCACGGTGGCTCACGCCTGTAATCTCAGCAC

The following amino acid sequence <SEQ ID NO. 170> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 42:

FPLQYHVLSEHPLLLKSHHDLIVWDIFGLALFCSFVTFHTVLSKTHQSSSLHWLHGCWSLCGLWQTTLSIP
PLPGQNSDFVRDSRVPGKLDFLGSFGVKVAKKLSPGQCFVSRHLWAGLLETLLFFWSGRVLFIPHVSLFWF
GKRTTLAAFQKAEGALILKSLQTCCSMGRTDLYWVKPLWLAVLHAAKYDYYVRCFSELILIAKQFKHVWGL
NGIRAGHGGSRLSQH

The following DNA sequence Seq-2501 SEQ ID NO. 43> was identified in *H. sapiens*:

TTTGTTGGCATTTTCGATATAAAATACCGAGGGCAGTATCAGGAAGTATGCCTTGCTGTGGATGGAGAGCG
TGCAGTGCCGCCTCATGGGGTTCCTGGCCATGCTGTCCACCGAAGTCTCTGTTCTGCTACTGACCTACTTG
ACTTTGGAGAAGTTCCTGGTCATTGTCTTCCCCTTCAGTAACATTCGACCTGGAAAACGGCAGACCTCAGT

CATCCTCATTTGCATCTGGATGGCGGGATTTTTAATAGCTGTAATTCCATTTTGGAATAAGGATTATTTTG
GAAACTTTTATGGGAAAAATGGAGTATGTTTCCCACTTTATTATGACCAAACAGAAGATATTGGAAGCAAA
GGGTATTCTCTTGGAATTTTCCTAGGTAAATTATATTTTTTCATTTCCTGGAAAAACATAATTTTGCTAGA
AATACGTTAAATTTCAGCAAAGGTGGATTTGTTTGTTTCAGAAAGTGAGATAACATAGTCAAGACTGTGTC
CTTTTTCACACAAAAAAGTTTTTACTATTGTGTTTATTGAAGTTTTATTAAACTTTTTATTAGACAATATT
TAGTGTGGAAAATAAAGACATACT

The following amino acid sequence <SEQ ID NO. 171> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 43:

LLAFSINTEGSIRKYALLWMESVQCRLMGFLAMLSTEVSVLLLTYLTLEKFLVIVFPFSNIRPGKRQTSVI
LICIWMAGFLIAVIPFWNKDYFGNFYGKNGVCFPLYYDQTEDIGSKGYSLGIFLGKLYFFISWKNIILLEI
RISAKVDLFVSESEITSRLCPFSHKKVFTIVFIEVLLNFLLDNICGKRHT

The following DNA sequence Seq-2502 <SEQ ID NO. 44> was identified in *H. sapiens*:

ATGCTTCATAGGATGTTTTATTGGATTACAAAGAATTTTTTAAAAAAGAATTTTTCAAACAAGAATTTTTC
AAAATTAATTCATTTCCTTAATACATCCATTATTTATTTACTTTTATTTATGTTTTCAGTTTCCTTTAATT
GATAGAAAATTTACATGCAGTAAAATGCACAGAACTTCAGTATACAATTCAATTATTTTGGATAAATATGT
ACACCTAGGCAATTGACATCTCAATCAAGACACAGAACATTCTCAACACTCTGGAAAGATCCTTTGTGTCC
ATTTTAGTTATGCTTACTCCTATCACCAACCATGTTTCTGGTTTCTATTGCCATATATTAGTTTATCTTGT
CCTTGAATTTCACGTAAATGGAATCATACACTGTGTTCTCTTCTGTGCCTTCTTGAACTCAATGTAACATT
TTGAGATGCATTTTATATTACAGGATGTACCTA

The following amino acid sequence <SEQ ID NO. 172> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 44:

CFIGCFIGLQRIFKRIFQTRIFQNFISLIHPLFIYFYLCFQFPLIDRKFTCSKMHRTSVYNSIILDKYVHL
GNHLNQDTEHSQHSGKILCVHFSYAYSYHQPCFWFLLPYISLSCPISRKWNHTLCSLLCLLELNVTFDAFY
ITGCT

The following DNA sequence Seq-2503 <SEQ ID NO. 45> was identified in *H. sapiens*:

AATGTAGTTCTGCACTTATGGATTATCCTTTCTTGGTGAAAATTACATTAATTAATAATCACTATTCAGGT
AACTATTTGAATACATTTGCCTCTGTGCCAAGGAAAAATAATTACTTCCAAAATAAAAAGGTAGCAAAACC
TCCTCCTAATCCTACTAAGATAATCAGGATTCCCAGAATGGGATTGATTATAAGCCTCCATACAAACTCAG
CATTGTCTTTTATTTTTAAATCAGTTAGAGAAAATGCAGCTAGCTGTCTGACATTTTTTGTGTGTTTATAA
ACAAAAAAACTCACATCTTAGATCTGAGTAAAAGTTATCCTCATATGGTCTCTCTCTCTCTCATTATGT
AGGTTTTAATTTCCTTAGCCAAGAGGATACCTCATGTATATTATGAGATTTGTCAATTTATGAGCAGATGT
AATTTTATTTTCTGTGATCTTTCAAAAATTTTCTATGCTGGATAAACTACAAATAAACACAAACTTTCTTG
AAAGGAAAATATCTAGGATTTGTAAATATTAATTTTGAAAATGTTTTCTTTTTAATATTGCTGATTCTTAC
ACTTCATCCAAAGTACTTATTATATTTTTTAGGAGATATACAAGTTAG

The following amino acid sequence <SEQ ID NO. 173> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO.45:

CSSALMDYPFLVKITLINNHYSGNYLNTFASVPRKNNYFQNKKVAKPPPNPTKIIRIPRMGLIISLHTNSA
LSFIFKSVRENAASCLTFFVCLTKKLTSIVKVILIWSLSLSHYVGFNFLSQEDTSCILDLSIYEQMFYFLS
FKNFLCWINYKTQTFLKGKYLGFVNINFENVFFLILLILTLHPKYLLYFLG DIQV

The following DNA sequence Seq-2504 <SEQ ID NO. 46> was identified in *H. sapiens*:

CTGCTTAAACGACTCCTTACTCTGAGCTCCAGTTTTCTTAACCAGAAAATCAGCTATTGTTAATTTTACCT
ACTTAGGGTCTCTCTCTATTTTTCCTTTCAGTTCATGTTAATTTCTAAATTGCCATGTATAAGTAAGGGGT
TGTCAATTTACACCATAAAACCCCTTTATGTATCCAAGGTTTTCATAGGAAATTTAGGACTGTATGATCCT
AAATTGTGCTGGAGTACCACATTTTCTGTTAAGTAGTACTTGGCAATAAAGTATAGGAAAAAAAAATCAGT
GGGTTGACAAAGAGAGGTCATGATAGTGTACCTGTAATGTAATTTGATAAAAAATGTGAGCCTGAACTGAT
TGCAAAGCATTGTTACATATAGGGGAAGACATTATGGGGGCAGAGGGGGGTGAAGATACAAAGTTGAATAA
AACTTCTCTAGAGCTTCACAATCTAATAAGATAGGCATTTATAAATATCTCTTAAGGCGCACTTTGTTAAG
TGCTAAAATAGTGGCACAAAGAGCTATA

The following amino acid sequence <SEQ ID NO. 174> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 46:

LLKRLLTLSSSFLNQKISYCFYLLRVSLYFSFQFMLISKLPCISKGLSIYTIKPLYVSKVFIGNLGLYDPK
LCWSTTFSVKYLAIKYRKKKSVGQREVMIVYLCNLIKNVSLNLQSIVTYRGRHYGGRGGRYKVENFSRASQ
SNKIGIYKYLLRRTLLSAKIVAQRAI

The following DNA sequence Seq-2505 <SEQ ID NO. 47> was identified in *H. sapiens*:

TTTTTAATTCTAGTAACTGAAGTTTTAGAAGGGTGAGAGTTTGTTTATGTGTGAACATTATAGAGACTCAT
TCAATACTGTATAATTAGAAGTTTAATCAGGTCAGTGGAGTGTAAACCATTACACAGGAAGTACAGCTCCT
GAGGCAATAGAATTCTTATGTAGAAATGTATACTTATTACCTAATCGAGAGTGTTTGGGTTTGCAGTTTAC
TAAAGTGTACAACAGCCAATGGCTTTTATATGTTATGTGCAACTTGTTTAGCCCATAAACTATACTAAAGT
GCATAATAAGACATTCAACTACATACGGTTACTCATTCAAGTCTGTTATCGATTGAACTGTACATAAAATG
ACATTTGCAGGATAGTGTATCCTTTTATTTATTGTAAGGTTTCTTTGTTTATGTATCAGCACACAAAATTT
AGTAATTAGCAATAGGTCTCAGTTCATTTAATGTGAATGAGCAAGATCTCAGCTCTTACTACATTCAATTA
TGGTGTAATAGCTCTCTTGACCTCCACCT

The following amino acid sequence <SEQ ID NO. 175> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 47:

GGGQESYYTIIECSKSDLAHSHMNDLLLITKFCVLIHKQRNLTINKRIHYPANVILCTVQSITDLNEPYVV
ECLIMHFSIVYGLNKLHITYKSHWLLYTLVNCKPKHSRLGNKYTFLHKNSIASGAVLPVWFTLHPDTSNYT
VLNESLCSHINKLSPFNFSYNK

The following DNA sequence Seq-2506 <SEQ ID NO. 48> was identified in *H. sapiens*:

AACCGCACTTTTGTACCACAGGGACATGCCAGGGAATAGCTCACATCAAATGCTTTCGGGAGGGGTGCCTA
TGAGGAAGAGGCCGCAGGTCAGCCAGACAGCTCAAAGGTACCATTAAGATGATGGACGCCTTTTTCCTTGG
TGCTTGGGCAGGCTGCTGAGCTTCATTACTCATCTCTTCCGCAGGGAGGTCACCATGCAAAGGGGGTGTCT
TGTGCTCCTCTAGCCAGGATGCAAGCCCTGGGGACCACATTCACATCCTTGGGAACAGAGGATGTGGGAGC
AGAACTTCAGATGCTCTAACTCAAAGGGAGCCTGGCCGCTCAGTGTGTCCCTGCCTGAAAGCAGGGCTCAG
GCTAAATGAACACAGGCCCCTTCCAGGCCACTGTGGCAAGTCACAACCTCTCTCCCCACCACTATCACCTC
TCCCCCATACCAGCAGATTCTTGACAGCCTGCAACTTCCTATCAAGGGAAAACCGCCAAAGGCAAAGCCAG
ATTTCTGACCAATTTTGAAATGCCTGAACAGGGAAGGGCATAGTGGCTTCATGTCTATAATCCCAGCATTT
TAAGAGA

The following amino acid sequence <SEQ ID NO. 176> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 48:

TALLYHRDMPGNSSHQMLSGGVPMRKRPQVSQTAQRYHDDGRLFPWCLGRLLSFITHLFRREVTMQRGCLV
LLPGCKPWGPHSHPWEQRMWEQNFRCSNSKGAWPLSVSLPESRAQAKTQAPSRPLWQVTTSLPTTITSPPY
QQILDSLQLPIKGKPPKAKPDFPILKCLNREGHSGFMSIIPAFE

The following DNA sequence Seq-2507 <SEQ ID NO. 49> was identified in *H. sapiens*:

GCAGCCTTTTCCGCGCTTCCCCGTGTCTGACTGTGCTGAGGGCCTCCTGAAGTGCAATTGGTTAGTCACGG
TTTAGTGTTCTTTACTGCAATGCTATTTTAAGATGCAATTAAAACGTCTCATTGCCAAAGTGCGTGCTTCC
TCCTGGGGGCCTCCTTCCTAACACGAAGGAGTCAGAAACCAAGGCCGGGAGGAGACCTGAGCTGAAGACTC
ACTTCTGGAGTGGGCACACTTTGTCCCAGCTCCGTCTTCCTGGAGCACCCAGGAGAGCCCGCTGCAAGAAG
AAGCCCCACGGCAGGCCACGTGGAGGCGAATTCACCTCCTACCCAGACAGCGTGGGCAATGCTGAAACGAG
CGTCAGCTCCGAACGATTTTAGTGAGGTTCAAACCTCCCCTCGGCTGTCAGCCTCTGAATCTCTTCCACTT
CAGCCACGGCCACTCCATGGCTAGGGGCGGGGAGGGGACACTCAGAAGTTTGGTTTCTTCTGAGGGGCCTG
AGCACACACTCAGGATGTGAGTGGGGCCGGGAAGGGCAGCAAGTGGAGCCTATGCAGGAACACTTGTGCAA
GGCTGCACGGTTTCACTACCACCAGAAGGCAACTAAAAATCCCCACAACTCCAGGTGTGTCCTGGCTGGTG
TCACGGAGCCTCACACACGGCTGAACCGCTTAACTCACA

The following amino acid sequence <SEQ ID NO. 177> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 49:

AAFSALPRVLCGPPEVQLVSHGLVFFTAMLFDAIKTSHCQSACFLLGASFLTRRSQKPRPGGDLSRLTSGV

GTLCPSSVFLEHPGEPAARRSPTAGHVEANSPPTQTAWAMLKRASAPNDFSEVQTSPRLSASESLPLQPRP
LHGGRGGDTQKFGFFGAAHTQDVSGAGKGSKWSLCRNTCARLHGFTTTRRQLKIPTTPGVSWLVSRSLTHG
TALT

The following DNA sequence Seq-2508 SEQ ID NO. 50> was identified in *H. sapiens*:

AAATATAACTACATAAGTATATATATGTACAGTTTAAGGAATAATAAAATGAACATCCATGTATTCAGCCT
TCCGTCTTTTTTTTTTTTTAATACCTTGCTGAATTCAGTTTGAGGCTTTTAAAAATTTTATATTTTTACATC
TCTATTTATGAATGCTGTTAGCCACCTTAGGTTACTTTTTATCCCCCATCCTTATCTGATTTGGATGTTAA
AGTTATATTAGCATCATAAAAAGGGAGTCCGATGTTGGACATTCTTATTCTGTTGTATGCAACCTGAATTA
TTCAGAGATTTCTAGGGTTTTATCTCTCCCTAGTATGCTGCAGGTTCACTGTTGTGGATCAAACATGGATC
ATTTTTGTTCATTCTGCTAAATCAGTATTTATGATAATCAGTATTTATCATAAATACTGATTCAGTAAATA
CATAAATACTGATTCAGTGGGCCCTTGAATCTAAAGATTTGTCTTTAGCTCTAGAAAACATTAATTTCTTT
TGAGTATGACTGCCCCACATTTCTTTTTGGTTTTCTCCTTGGGAAATTTGTATTAGATAGATGTTGGGAAC
TTTGGGACATATGCCTGCATGTCT

The following amino acid sequence <SEQ ID NO. 178> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 50:

KYNYISIYMYSLRNNKMNIHVFSLPSFFFLIPCIQFEAFKNFIFLHLYLMLLATLGYFLSPILIFGCSYIS
IIKRESDVGHSYSVVCNLNYSEISRVLSLPSMLQVHCCGSNMDHFCSFCISIYDNQYLSILIQIHKYFSGP
LNLKICLLKTLISFEYDCPTFLFGFLLGKFVLDRCWELWDICLHV

The following DNA sequence Seq-2509 <SEQ ID NO. 51> was identified in *H. sapiens*:

TTTAATCTGGCCTATTTCTTGGCATATCAGTGTGCACTCGATAAATGTATAGTAATTAAATTTTCTTAGCC
AGACAATTGCTTGAAGTTTAAATCCAGCCAATAAAATAAAAATAGAAAGCTTAGTTGTTTGTTGTAATGGA
TAAAAAAATGACAGCACAGGTGGTAAGCATTCATATAGATCAAAGGCAGAGTTTTCTGTCTTGCTATGCAA
CACAATCACCTGAATATCTGATATAGTAAACACTCCTGGGTAATTCCAATATGCTGCCAAGGTTGAGAACG
ACTCAAACTTTCAGCACCTCTGGGTATTACTATTACATACTATAGCACACAGTTAGGTGTGTTATATCAAA

The following amino acid sequence <SEQ ID NO. 179> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 51:

LIHTLCAIVCNSNTQRCKFESFSTLAAYWNYPGVFTISDIQVIVLHSKTENSAFDLYECLPPVLSFFYPLQ
QTTKLSIFILLAGFKLQAIVWLRKFNYYTFIECTLICQEIGQIK

The following DNA sequence Seq-2510 <SEQ ID NO. 52> was identified in *H. sapiens*:

TCTGCAAAATGCCTTTATCAAATGGCTTGCAAGATTAAGATGGAGTATTTATTAGTTAACCCACACACAGC
AAGCAGAGGGGAGTGGAAATTCATGATGTACGGGATGTCCTGCCAACACTGCACGGGATGGTCTACACATC
TCTGATTGCAATAACACAACCAGTCTGATAATATTCTGTACATGGACTCATAGCATATTTTATGGCTTACA
AAATAATAGTCAAATGCTAATAAATAATTGACTTGAAAAAACTGAGGACATAATATAAAAGTAATACTATT
TATTTTATTCATTGCTCTAAAATAATTTTATAAATTTGTCTACTCATGTTCAGCAGTGGAGTTCTGAGATT
AATTTTATTTTCCTTTCATAAGTCAAGACAATGGGGAATTTTAATTCTGTAAAGACTCAACATCCTTCCTC
TCCACTTCATTTGGTAATTGTCTTCTTTCATGACTGAATTCCTCTTAGTCTTAGCCTGAGTCCCACTTTGT
GCTTATTCCACAATGATGTCTGCTGTGAGGCCATTTCCTTATCAGGGTCTCCAGACTATTTTCAGAACATC
ACTCGTGTCATTTTTAGTTGCTGACAATTCACTTGAACTACAGAGTCTTTGGCAGCTGCATCAAAAGGA

The following amino acid sequence <SEQ ID NO. 180> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 52:

LLMQLPKTLFKIVSNKHECSENSLETLIRKWPHSRHHCGISTKWDSGDEEFSHERRQLPNEVERKDVESLQ
NNSPLSLMKGKNSQNSTAEHETNLNYFRAMNKINSITFILCPQFFQVNYLLAFDYYFVSHKICYESMYRIL
SDWLCYCNQRCVDHPVQCWQDIPYIMNFHSPLLAVCGLTNKYSILILQAIRHFA

The following DNA sequence Seq-2511 <SEQ ID NO. 53> was identified in *H. sapiens*:

GAAGTGGGATTCCATCTTCCGCAATGTATGTATTCTGTGATATGATTTTGGTTGAAACTTGTGAAGAAAAT
ATGGAAGGAAGAAGAATTTAATACTCTTCTCAGATAATTGTGGCTATTCTTTTAAACCTCACAAAAGCTTG

ACAAATCGTATTTTCTCAAAGGTCAGTTATAATGTTGAATCTGTAACTGTACTGATGACCTTCTTCGTACT
CTGTTATATTAAAATCTCTTGATCTGTGTTACACTTGGATAGAAATTTTTTCGCATCATTTTGTACTAGCT
TGCATGAGTTATTTGGAAACTATTAGCTCACTGACTTGTGCTAATCTTACAAATGTTGACATGTTTCACTA
TACAATATCAAAATTGCATTTGTCAATATCATCATCACCTTAGCCTCTAAGGATTGGGATGCTAATAAGCT
TACAGTATAAGATGCAACTTTTTTCCCCAAACTTGAGTTTTGTCATTGGCAACACATTCTGCCAGTTATTT
TCCTTGAAGTGACAGGCTAACTTTGTTATTTTCTTAAGAGAATGTGTGCCAAATATCCAAGTCTGAGTAAC
CATAGTTCGTCTGTCAGTGGTTTTTTAAGTGGAAATGATGTTCCATTAAAAAAAGTGGCTAATTCATCTCA
TAACTCAATCGTGTAAGTACTTTTCCTGGAAGTGACCATTC

The following amino acid sequence <SEQ ID NO. 181> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 53:

KWDSIFRNVCILYDFGNLRKYGRKKNLILFSDNCGYSFKPHKSLTNRIFSKVSYNVESVTVLMTFFVLCYI
KISSVLHLDRNFFASFCTSLHELFGNYLTDLCSYKCHVSLYNIKIAFVNIIITLASKDWDANKLTVDATFF
PKLEFCHWQHILPVIFLEVTGLCYFLKRMCAKYPSLSNHSSSVSGFLSGNDVPLKKVANSSHNSIVVLFLE
VTI

The following DNA sequence Seq-2512 <SEQ ID NO. 54> was identified in *H. sapiens*:

ACCCTCCCCCCAATTCAATTACCTCCCACCATGTCCCTCCCACAACACGTGGGAATTCAAGGTGAGATCTG
AGTGGGGACAGAGTGAAACCATATTAATTATATAATCATAAGATTGTAAACTCTATGAAGCCAAGAAATAT
GTGTGATTTTGTTCACCATTATATCTCAAGCACTTGGCATAGTATCTGGCATGAAATAGATGCTTAATGAA
CTATTTGTTTAATGGATGTTGATCATTTGTGTTGGTGACTTTACAAGGTTAACATTTTTTTCCATGTTGAG
GACATGGGCAAACTGTCCTATGGCTTGTGGCTGTGATGATGCATGGCAGCACTGGGGTGCTTCCGACTGGT
CTGCTAAAGACTATTAATAATTTTTCTATATCTGCCAATAGGAATCTTATTTATTTTTGTCTGTGGCTGTG
TTTCCTGTTCTTCAGGGCACAGTGAAGCCCCATTTGCCTCAAGTTGTTTTTCTAATGATTTTCCTTTGCCC
ATATCCTGAACCAATTTCTGGTGTATCAAATTTCCACAGAAGACTGTACTCAAGATGGCAGACCAAAGCAC
ACATGCTGATCTACA

The following amino acid sequence <SEQ ID NO. 182> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 54:

PSPQFNYLPPCPSHNTWEFKVRSEWGQSETILIISDCKLYEAKKYVFCSPLYLKHLAYLANRCLMNYLFNG
CSFVLVTLQGHFFPCGHGQTVLWLVAVMMHGSTGVLPTGLLKTINNFSISANRNLIYFCLWLCFLFFRAQS
PICLKLFFFSFAHILNQFLVYQISTEDCTQDGRPKHTCST

The following DNA sequence Seq-2513 <SEQ ID NO. 55> was identified in *H. sapiens*:

ATAATATACTGAAAATTCAAATTTTGATTACTTTTTCAGAGTTAAATGGTTAGCAATCAAACAATTGATTA
GAAGCTTGTATCAGGTAAAAATAGGATATTTAGTGTAAATATGATTTTCTTTACGGTCCTTGATACATCTT
TTCACCATTTTCAACTGAAATATATATGTAAACATAGGGGGTAGGGACCACAATCAACTGCAGAGAATCTT
CATGTAATCATAAGATCGACTGAGTTAAATAAAAAAAATCAAATTCTGTGAGCAACACATAATATATGTTC
AGGATTAGAATAAAACTATCTGCATGAAAAATGTTTAGAAGAACCTCTATTCATCCACAAATATCTTCTCC
TTGTCCACAAACCAGGGTTTGTGCAAGCCTGGAAATTAAATGGCATACCCTTTCCTGAGTGCTACTATTCC
TGAGTGCTACTAGGCCAGGGATTTGGCCTAGGTACTGTTGCTCGCAGCACAGAAAGCCAATCACTGAGACA
AAGAGTAGTGCCAAGGAAGAAGGCTTTAATTTGGTGCTGAAGTCATGGAGACAGGGAGATAAAATCTCAAA
TCTGTTGCCTCAGTTGACTAAACTTAAGGGTTTATACAGCAGGGGGAAAATATAAGTATGTGTGAG

The following amino acid sequence <SEQ ID NO. 183> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 55:

HTYLYFPPAVTLKFSQLRQQIDFISLSPLQHQIKAFFLGTTLCLSDWLSVLRATVPRPNPWPSSTQEHSGK
GMPFNFQACTNPGLWTRRRYLWMNRGSSKHFSCRFYSNPEHILCVAHRIFFLFNSVDLMITRFSAVDCGPY
PLCLHIYFSKWKDVSRTVKKIIFTLNILFLPDTSFSIVLLTILKSNQNLNFQYI

The following DNA sequence Seq-2514 <SEQ ID NO. 56> was identified in *H. sapiens*:

TTACAAAAGGAAAATATTCATTCTTTTTTGTATATTTTTATGATGATTAGGGTTTCTAATACAAAGGAAAG
CATTCTTTTGTATTTGAAACCCTATCATTGTGCTTGCTGAATTGAACATTGCTGATAACACCAGAAGACCC
CTACATTCTCTACTCAATAGGAGAGCTAATGAGGTGGCATGTGATGTAGATCCATAGTATGTAAGAACACA
GGACACACACACACACACACACACACACACACGGCTTATTAATAATGTAATGTTAAATAATACAATGCAGG

GCATTTACATTGAATGACGGTTTTGTTTACAGCAGATTTGCTGGTTCAGAAGGGACCAGTTGATCCACTTA
AACTATTTTACTTCTTGAGTAGCCCTATTTCTGTTTTGTCCTTTTTCCCCCCAAAAATTTATGGCCAGGAG
CTACC

The following amino acid sequence <SEQ ID NO. 184> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 56:

LLAINFWGEKGQNRNRATQEVKFKWINWSLLNQQICCKQNRHSMMPCIVLFNITLLISRVCVCVCVCVSCV
LTYYGSTSHATSLALLLSRECRGLLVLSAMFNSASTMIGFQIQKNAFLCIRNPNHHKNIQKRMNIFLL

The following DNA sequence Seq-2515 <SEQ ID NO. 57> was identified in *H. sapiens*:

TTTAAAATGTATGAATACTCTCCTTCACTGGGAGGATCAATTGGATCAGAATCTCCGAAGGGTGATGTTCA
GGTACCGATACATATTTTAGGAGTGCCTTGATTATATTACATAGCTGGGATTGAGAATTGTTGATGTAGGT
TATCTGGGCAGCCACCCAACACCATACACCACCACCTGAATGCAGTGCTGCCATTGCATTTATATTTATAC
TCATATTTGTAACAAATAATCTAGTAACACAATGATATTTAACTTTTCATGTTTCAGTAAGTATAACTGGC
TATCATTAAGCTGCTCTGTTCTATTATCAGAACGACAGATTTACAAAGGCAGCCTTTTATTCATGTTGAGT
TATTTTTCCAGTTGTAAAATCACCTCCCACCCTTTTATTGTGCTAGTCATTCAAAACTAGAAAATATTTTT
GGAGGAATAACACTGGAGTTTAACAAATGACTTTTTAAAAATTAGACTTGCAATAGCAAAAACAACATAAA
GTAAATATTATGCATTTTAAATGTTTCTGGCAACTAAGAAAGGAACAGAGACAGACATGAAATGAAAACGA
CGAAATTGTGGCAGGTGAAGTTCCAATGACCTTGGAAAATGTTACCAGTAATACTTCACAATATATACCAA
GTGATGGGAAAA

The following amino acid sequence <SEQ ID NO. 185> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 57:

FPSLGIYCEVLLVTFSKVIGTSPATISSFSFHVCLCSFLSCQKHLKCIIFTLCCFCYCKSNFKVICTPVLF
LQKYFLVLNDHNKRVGGDFTTGKITQHEKAAFVNLSFNRAAPVILTETKVKYHCVTRLFVTNMSININAMA
ALHSGGGVWCWVAAQITYINNSQSQLCNIIKALLKYVSVPEHHPSEILIQLILPVKESIHTF

The following DNA sequence Seq-2516 <SEQ ID NO. 58> was identified in *H. sapiens*:

ATTGCTTATGAAATGTATTAAGAAAATTGTGTGCTTAACAAAAACAAACTTATTCAGGTTTGATGGTTTGC
TGATCTACACACACACACACAAAATGGCCCTTTTCACAAAGCAGTTGGCTTTCATCAACTTCTCCATAATG
CCATACATGCATACAAATCACACTTTCAGTTATTCACTGTAGAAATCTCATCAATAAGAAATCCCTTGTGA
TAACTGGGCCTTCATTGGCTTTCTTTTATTGGCCAAATGCTGAGTATTTTTGGCTTGAGATGATAACTTTA
TTTTAAGCCTGAGAGAGCAGGTGACTTGCCCTTGGTCTAATGATACTAAGCAGCTGCCACAGCCTGTTTCA
CATCCACTGGAGAAGACTGTTCCCTGGAGAGGGAGCACATAACTGTGCATGTCTCTTTCAAGATGTCTCTT
TGGGTACCATGTTGGGAAGTGACTTTCCAAGGGTGAGGAGTGCCCTGTGTTTAGCTTTTTGGTTACATCCC
TGTGCACAAAGGAGAGACCGTGTTAAAGAGTTGAGA

The following amino acid sequence <SEQ ID NO. 186> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 58:

CLNVLRKLCAQKQTYSGLMVCSTHTHTKWPFSQSSWLSSTSPCHTCIQITLSVIHCRNLINKKSLVITGPS
LAFFYWPNAEYFWLEMITLFAESRLALGLMILSSCHSLFHIHWRRLFPGEGAHNCACLFQDVSLGTMLGSD
FPRVRSALCLAFWLHPCAQRRDRVKELR

The following DNA sequence Seq-2517 <SEQ ID NO. 59> was identified in *H. sapiens*:

TTCAAAAGTGATCTCTAAATTTCGAAAGAAATCAGATATTCAAGGGCTCTGGTAGGAGCCTTTAGTCCTTT
ACTCACGTTTTTACTGACTATATGAACTTGCACATAATCTGTCTGTAATCCAAATGAAATGGTCTAATGCA
CAAACATATTGTTTTCAAGAAATACCAGAACTTTTCTCTGACTGACTAAAGGTTATTAAAAATGTTTGTTC
TAAAATCATTTCTAATTTTTGATTTAAGATGTCTGGTCTCTCCCTTCCCTTCTTTGATAAATAAGGCTGCT
ACATTTCCTAATTTTTCTAGATGTTTACGCAATATAATAATGATAAAATCTAAATAATGGACGACAAAAAA
TTAATGTTACAAAAGGAAAATATTCATTCTTTTTTGTATATTTTTATGATGATTAGGGTTTCTAATACAAA
GGAAAGCATTCTTTTGTATTTGAAACCCTATCATTGTGCTTGCTGAATTGAACATTGCTGATAACACCAGA
AGACCCCTACATTCTCTACTCAATAGGAGAGCTAATGAGGTGGCATGTGATGTAGATCCATAGTATGTAAG
AACACAGACACACACACACACACACACACACACACACGGGTTATTAATAATGTAATGTTAAATAATACAAT
GCAGGGCATTTACATTGAATGACGGTTTTGTTTACAGCAGA

The following amino acid sequence <SEQ ID NO. 187> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 59:

LLTKPSFNVNALHCIIHYIINNPCVCVCVCVCVCVLTYYGSTSHATSLALLLSRECRGLLVLSAMFNSAST
MIGFQIQKNAFLCIRNPNHHKNIQKRMNIFLLHFFVVHYLDFIIIILRKHLEKLGNVAALFIKEGKGETRH
LKSKIRNDFRTNIFNNLSVREKFWYFLKTICLCIRPFHLDYRQIMCKFISVKTVKDRLLPEPLNIFLSKFR
DHF

The following DNA sequence Seq-2518 <SEQ ID NO. 60> was identified in *H. sapiens*:

CTTGATCACAGGTTATCCTAACAGACACAATAATAATAAAAAGGTTAGAAATATTGCAAAAAGTAGCAGAG
GCATGAAGTAAGCACATGGTGTTGGAGAAATGGCTCTAAGAAACTAGCTCGATGTAGAGTTGCCGTAGTCC
TTCAATTTGTAAAATATGCAATGTCTATGAAGCACAATAAAGCAAAGTGCAAGTAAACAAAGTACGCCTGT
AAGTGCTGATATAGTAAGCTTAAATTTTCATTATCACCACCCCTTGCCAGGTTTGTAGTTTTTGTCTTTAT
AATATCGTCTGTATATGAAACAAAGTAAAATCTGTTTTATTTCTTATAAAGCTTTCCCAGAGTATCTAGTA
TAATTCTGTGCATGTAGAAGACTTCTCAGTAATTATCCACTACTCAAGAGACAACCTGCTGTGTGGAGTGA
CTGAATCCTAGTGAGCCTGCCCCACAGTGGCCGCA

The following amino acid sequence <SEQ ID NO. 188> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 60:

CGHCGAGSLGFSHSTQQVVSVVDNYEVFYMHRIILDTLGKLYKKNRFYFVSYTDDIIKTKTTNLARGGDNE
NLSLLYQHLQAYFVYLHFALLCFIDIAYFTNRTTATLHRASFLEPFLQHHVLTSCLCYFLQYFPFYYYCVC
DNLS

The following DNA sequence Seq-2519 <SEQ ID NO. 61> was identified in *H. sapiens*:

CCCGCCTTGGCCTCCCAAAATGCTGGGGATTAGGAGGCGTGAGCCACTGTGCCCGCCCAGGACTCCACCAT
TTTACAATAAAAAATAACATTACCATATCATCAAATAATATGTGATTATTTGATACTTAAAAATAGTACAG
TATGCAGATTACTGGAATAGTGAAAATTGATAACGCAATCCCTAGTAGAAAGAAAATCCGAAAGAGTTCTG
TATACCGGCTTTCAGTACATTTAAATATATATATGTTTGAACAATTCATCTTTATCCCTAATACAATAACT
TTTCAAAAGCTAATTTATAAATGTCAGTTTGTACAGATACAAACTGTATAATATCCAATATAATCAGATAT
TCTCAGAATATACAGATTAAATATACAGAAATAAATGTATGGTTATTGCCTGATCATAATTCCTTAGGGAA
GGCAATAATTCACAATTTATGTACCCACAGTGGCAGTGTAGAGAGGTGGTTTTGCCAGTGATTACTTAATA
CTAAGTTGCCAACACAGTACTTAAAACCTTCATTTATGAGAGTCTAAGAGATCTCCTTCCTGGAAATTATC
AAGTATGCATCGAGGCTACACAATAGAAAGAAATTAGCTTTTAAAACAATGATGCAGTCCGGTTGCAGTGG
CTCACGCCTGTAATCCCAGC

The following amino acid sequence <SEQ ID NO. 189> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 61:

LGLQAATATGLHHCFKSFLSIVPRCILDNFQEGDLLDSHKRFVLCWQLSIKSLAKPPLYTATVGTIVNYCL
PGIMIRQPYIYFCIFNLYILRISDYIGYYTVCICTNHLISFKVIVLGIKMNCSNIYIFKCTESRYTELFRI
FFLLGIALSIFTIPVICILYYFVSNNHILFDDMVMLFFIVKWWSPGRAQWLTPPNPQHFGRPRR

The following DNA sequence Seq-2520 <SEQ ID NO. 62> was identified in *H. sapiens*:

AACAATCCCAAATAATGTAACAGATATAAAATATTAAATGCTAATATTTAATACCCTGATCATAGTAGGTC
CTAAATAAATGGTACCGAGTGCTCATTCATGTAATACCCTGATGAAGAAAGTAAGTTGCAAAAATAATTGC
TTTCTATTATGTAGCTATACAGAGATGAGACAGTTCCTACTTCCTTAATTCTTAAAGGAGCAGAAGAGTAT
GGCACCAGGAATAGAACTTGGGGCACAGCAGGTTCCTTTCTACTGCAGAAAAAGGCCATTCTGAAGCCACT
TATAGTTACTTCTGTCTCCCAGAGCCTTTTCTGTGCATATGAGGTCAAGGTCAGTGTCCATGGAGCCTGGA
AGGCTGTTCTGAAGAGAAAGGAGAGCCATGGGTTCACGCAGGAGCTGGAGTGGACAGTCCTGGCGGGGGAG
CTGGGTAGGGTATGATGCTGGGCATGTTCACTGTGGCTAGTTAGTTCTGGGGTACAGGCATCCAAAATGCT
CAGGTGCACATCACAGAAGGGAAAAGGAAAGAAAATCTCGGTCATGCTCCTTGGAGTTTCCTCAGAGAACA
AGAATTTACAGCACAGCTGAATTAGGGCAGAGAAAAAGACCACCGAGTGCTTGTCCCTTTTTGTGGGCTCG
GGGGAAATGC

The following amino acid sequence <SEQ ID NO. 190> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 62:

ISPEPTKRDKHSVVFFSALIQLCCKFLFSEETPRSMTEIFFPFPFCDVHLSILDACTPELTSHSEHAQHHT
LPSSPARTVHSSSCVNPWLSFLFRTAFQAPWTLTLTSYAQKRLWETEVTISGFRMAFFCSRKEPAVPQVLF
LVPYSSAPLRIKEVGTVSSLYSYIIESNYFCNLLSSSGYYMNEHSVPFIDLLSGYILAFNILYLLHYLGL

The following DNA sequence Seq-2521 <SEQ ID NO. 63> was identified in *H. sapiens*:

TAAATTACAGTCTGTAAATAAGAGGTAGACCATAATTGCCATTCCTTAGGTATAGACTATCCATAGTGATT
GTCTTTCCAGACAATGTGGTATAGAAAGGAAGAACAAAAGAGAAGAAATTCATAGTGAAACAACCTGATAA
ATAACTTCTCAAGCCAGCTGACCAAGGTTAACATTAACAGTGATTAGTTATATTGACTGCATGCACTTTTA
TAGGAGGCGATATAAACAGCACTTCCTCATCTCTACTGTCTTCCTCCCAAAAAACCTTACCCCAGGCTAAT
CATGAGAAAACCATGAGACAAAAATACCAACTAAAAGCCATTCTATAAAATACTTGTCCAGTAATCCTCAA
AAATGTCAAGGTCTTCAAAAATAAGGGAAGCGTGAGAAACTGTCATAACTAATAGGAGCCTCAGAAGATAC
AACTACTAAATGTAATGTATTCTAGAGGAGCTTTTGACATGTAAAATGAACATTAGGGAAAACCTGGGGAA
TTACAAATAAACTATGGACTTAAGTTGACAATAATGTATCAAGATCAGTTTTATTAATTGTGATCAGTGTA
CCAGGATAAAGTTTTAAAAATAGATCAGGGCACATTGGTTCATGGCTATAATCTCAGCTCCTTAGGAGGCT
GAGGAGAGAGGAGT

The following amino acid sequence <SEQ ID NO. 191> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 63:

LLSPQPPKELRLPTNVPSIFKTLSWYTDHNNSYIIVNLSPFICNSPGFPCSFYMSKAPLEYITFSSCIFGS
YLQFLTLPLFLKTLTFLRITGQVFYRMAFSWYFCLMVFSLAWGKVFWEEDSRDEEVLFISPPIKVHAVNIT
NHCCPWSAGLRSYLSGCFTMNFFSFVLPFYTTLSGKTITMDSLYLRNGNYGLPLIYRLF

The following DNA sequence Seq-2522 <SEQ ID NO. 64> was identified in *H. sapiens*:

TCAGCCTCCTAAACACTTTTGTACTGTACACCCCTCAACCCCTGCCAAACTCAAGGAATTATAAACTCACA
AATAGCTCCATCAGCTTCTGCCTTTAAGGTTCAGTATTAGTTTTCTAGGGTTGCCAACAAATTAACATAAA
CTTGTTAGCCTAAAACAACAGAAATTTACTCTCTCATAGTTTGGAGACCAAAATCAAGGTGGTGGCAGGGC
TGCATCCTCTCCAAAGGCTCCATTCCTTGCTTCTTTCAGCTTCTGATGGCTCCACATATCCCTTGGCTTGT
GGCTACATCACTTTCATATCTACCTTGGTGGTCTCATGGCCTTCTGCTCTTCTAGGTGTGACTCTTCTCTG
TGTCTTTCTTTTATAAAGACATTTGTCATTGGATTTAGAGCCCACCTAGAAAATTTAGGATAATCCTACCC
TAAGATTCTTAACACTTACAACCTTAATTTGAGGGTCTGCCAAGCCTTTTTTTTTTTCCATATAAGATAAC
ATTTACAGGTTCTGGTAATTTGGACATGGACATTTTTTGGGTGGAGAAAGGTACCATTTAACCCAATACAG
CCTGTT

The following amino acid sequence <SEQ ID NO. 192> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 64:

SASTLLYCTPLNPCQTQGIINSQIAPSASAFKVQYFSRVANKLTTCPKTTEIYSLIVWRPKSRWWQGCILS
KGSIPCFFQLLMAPHIPWLVATSLSYLPWWSHGLLLFVLFSVSFFYKDICHWISPPRKFRIILPDSHLQPF
EGLPSLFFFPYKITFTGSGNLDMDIFWVEKGTIPNTAC

The following DNA sequence Seq-2523 <SEQ ID NO. 65> was identified in *H. sapiens*:

ATCCATTTAATGAAATGTCTATTATTTACCTGAATATAAGTTTAGATTCTAAATTATGACAAGTTTATCTA
CAAGTACTTATTTCATTACATTTCCATAATTATTTTATTTTAATAGTTTACCTAGATTATTTACGAAACCT
GCAATAGTTATCATTTAATGTTACTTTCCTGTCAACCATTTTATAGCTTGTGGATTTCAGGTGTTTACCCT
AAGTGAGAACCTTAAGTTTAGATACATGATTATTTTACAAAATAATTCAAGTTTTAGCTATTTTCATTAAA
CCAATATTAATGTCTTATTTATCAAAAATTACACAAGCAAAGGTCATTTCTGTTTTGGTCTGGGTTTATAT
TTTAATAACTCTTATTTCAAATTTTGACCCCTTATAGTATTTTGGTAGAGATACGTATTGAAGTCTCTTGA
CTCCAGAAAAGGGAGTTTTACAGAGAAACAAACTTTGGATGTCAACTAAATTGGGGAGATTAAAGATTCTC
TAGAGAAAGCGGGGGGCTCCAAAGCTTCAGCAATTTGTCCTATTGATTTGAGCCATAAAGA

The following amino acid sequence <SEQ ID NO. 193> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 65:

PFNEMSIIYLNISLDSKLQVYLQVLISLHFHNYFILIVYLDYLRNLQLSFNVTFLSTILLVDFRCLPVRTL
SLDTLFYKIIQVLAIFIKPILMSYLSKITQAKVISVLVWVYILITLISNFDPLYFGRDTYSLLTPEKGVLQ
RNKLWMSTKLGRLKILRKRGAPKLQQFVLLIAIK

The following DNA sequence Seq-2524 <SEQ ID NO. 66> was identified in *H. sapiens*:

TCTTATGTCTTTTGTCAGCCTTCATTGAACTGTGGTAAGCTAATTTGTTAACTTGCAAATAGTGTAAAACC
TTACACTCTTTACAGCTCTTGACAATAACTATATTTTCAACAACAAAATGATCTAATGAGAAAAGCGGCAT
TAACATTTTCTTGCAAATCTCCAATGTCTAGCTTAGTAGTAGAGAGCTGAGTTCTCGCATCTGATACATTC
TATTCTTGCAATATGTTGTTTTGGTTGAAATATGTGACAAAAATCTGGTCTCACACAGACATAT

The following amino acid sequence <SEQ ID NO. 194> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 66:

SYVFCQPSLNCGKLICLANSVKPYTLYSSQLYFQQQNDLMRKAALTFSCKSPMSSLVVESVLASDTFYSCN
MLFWLKYVTKIWSHTDI

The following DNA sequence Seq-2525 <SEQ ID NO. 67> was identified in *H. sapiens*:

TCGTCAGCTCTGCGCTCACCTGCTCTCTCCCTGGTCCTGCACACCAAACCTGTTCCTGCCTCAAAGCTTTG
CCCTGGGAGTATTCTTCCCCCTTGCAAAGCTGGGTCTTGCAAAGCTGGGTCCTTCCCATCATTCAGTTCAA
AATCACCTCCTGGGATAGATCTTCCCAGACCAACCAATGTGGAGTACCTTTCCTGCACCGGAGATGTTCCA
CCATTACATCACTATGTTGTATTTTACTTACACACTGATCATCTCAAATTATCTTGTGTATTCACTAATTT
GTTTCTTTTCTGCACCTGCCCCGTGCCACGCTGAGTGTTCATGTGGCGCCCGGCCTTGAGTGTTACTTTCA
CTAGCACAGCACCCATTTCTCTCTTGTGAATTGCTGAGACTCTAGTGCCCATTTCAGGACTCTGTCTTCAG
ACTTAAGGATAAGAGGAATAGACACTAGGGTGGGGGGAATGTATAGGCTATTAATATGAGATGAAAATGAA
AAGATTGCCAGGTAACACTGCAGTACAGTTGAAGTTAGATAGCACGAACTCTGTATTTTCCAAGACTTTCT
CCACCTACTCTTGACAGCCTGGGTGAGAATAGAAAGGTTGACAACAGAGACAACATAAATTTTGGGCAGAG

The following amino acid sequence <SEQ ID NO. 195> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 67:

VSSALTCSLPGPAHQTCSCLKALPWEYSSPLQSWVLQSWVLPIIQFKITSWDRSSQTNQCGVPFLHRRCST
ITSLCCILLTHSSQIILCIHFVSFLHLPRATLSVHVAPGLECYFHHSTHFSLVNCDSSAHFRTLSSDLRIR
GIDTRVGGMYRLLIDENEKIARHCSTVEVRHELCIFQDFLHLLLTAWVRIERLTTETTILGR

The following DNA sequence Seq-2526 <SEQ ID NO. 68> was identified in *H. sapiens*:

ATGCTGTCTTGATGAAGTTGGGAGGGACAGTTACCTAATGCTACCACTCTTGAGTTGTTCCTGGAACAAAT
CACAGTGGAGTCTGAGATGGGAGTGAAAACTAAATGATATCTGCAGCCTATGCAGCTGCCAGCCCTGTCCA
CTGGAGGCACCCACTTTATTCTTACTGAAATTGCCATCTGTTCAAATCCTCCGATCATTATCAATGATCTC
CTTTCCCATCTAAATTGTTGATTACTGTTAATTGAATCTTGGGACTATCTTTCAGTGCATGATTGAATCTC
ATTTAGGGAAGATTTATAGTCACTGGTACTTGAAGGAGAGGCACAGTTATAGTGGTTCCTTGGTATACATA
GGGAACTGGTTCCAGGACCCTTTGAGAATACAAAAATCCAAGCATATTCAAGCAGTCCCAAAGTTGGCCCT
GTGGAACTCACCTGTAAGAAAAGTGGGCCTTCCATATTTGCAGGTTTTGTATTCTGTGAGTACTCTACTTT
TGATCTGCATTTGGTTGAAAAAAATCTGTGTATAAATGGACCCATGCAGTTCAAATCCATGTTGTTCAAGG
GTCAATTGTATAGCTTT

The following amino acid sequence <SEQ ID NO. 196> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 68:

CCLDEVGRDSYLMLPLLSCSWNKSQWSLRWEKLNDICSLCSCQPCPLEAPTLFLLKLPSVQILRSLSMISF
PIIVDYCLNLGTIFQCMIESHLGKIYSHWYLKERHSYSGSLVYIGNWFQDPLRIQKSKHIQAVPKLALWNS
PVRKVGLPYLQVLYSVSTLLLICIWLKKICVMDPCSSNPCCSRVNCIA

The following DNA sequence Seq-2527 <SEQ ID NO. 69> was identified in *H. sapiens*:

AAGAAATTTCAGCTTCTGCCCACCACAAAAGAGACAATAGTTTGGAATCTGAATTCAGCCAAAGTTAACCC
CTTGCTTAAAAAAGAAAGGAAAAGAAAAGAGGAGAGGGGAGGGGAGGGGAGGGGAGACCAAAATTCAGCCA
AAATTAACTCCTTGCTTAAAAAAGAAAAAAAAAAGGAGAAAAGAAAAGGCCAAATCAACAACACGTTCAAA
GATAACAGAATCCAGTCTCCACACTATATCATTGTTCAGAATATAATTCAAAATTATTCAACATATGAAAA
AACAAGAAAAATCTAACCCATATTCAAGAGAAAACACAACCAATGGAGAAAAATCCAGATTTTTTTTAGTA
GCAAAAATCTGTAAGCAATTATTGTAAGCAGCTTAAGGACATAAAGGAAAATGTGCTCACAATGAATAAAC
AAATACAAAATGACAGCTGAGAAATGGAAATAAAAAAGGTCCAATGGAAATTATGGAACTGAAAATGACAT

TATTGGAAATAAAATATACACTTTCCAGTTATTTAAATCTTCTTTTAAAATCTGCCTTCTTTTATGTCCAC
ACCATAGTAGTGTTCACTAAATTCTTTTCTATAAAGATGGGATCTCACTGTGTTG

The following amino acid sequence <SEQ ID NO. 197> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 69:

QHSEIPSLKRITLLWCGHKRRQILKEDLNNWKVYILFPIMSFSVPFPLDLFYFHFSAVILYLFIHCEHIFL
YVLKLLTIIAYRFLLLKKIWIFLHWLCFLLNMGIFLVFSYVEFIIFTMICGDWILLSLNVLLIWPFLFSFF
FSFLSKELILAEFWSPLPSPPLSSFLFLSFLSKGLTLAEFRFQTIVSFVVGRSNF

The following DNA sequence Seq-2528 SEQ ID NO. 70> was identified in *H. sapiens*:
TTTTTTCTCTCATTTCCTCAATTACTACTTTCCTTTGTTTTTAGTTCATTTTTTATAGTGACACATTTTG
ATTACCTTTTTATTTCCTTTTGTGTACATTTTGTGGATATTTTCTTTGTGGTTACCATGGAGGTTACATGT
GACAGTACAAAGTTATAACAATCTATTTTGAATTAATACCAACTTGACTTCAATTGCACCCAACACTTTGC
TTTTTTACAACTTTCCCTTCCTGCTTTGTTATGTTATTTCTGTCAAAAATCAATCTTTATATATGTTGTGT
ACCTATTAACATGGATTTATAATTATTTTTGTGAATTTGCCTTTTAAATTCTTTAAAAAATAAAGTGTAGT
TACAAGCCAAAATTATATAAAACTATTAGTTTTTATAATGTCCATGTATTTGCCTTTACCGGAGATCTTTA
TATTTTCCTATGTGTTCAAGTTACTGTCTATTGTCATTTTATTTCAACTTTGAAGGGCTGTCTTAACACTG
ATTATAGTGGAGGACTAGTAGTAATGTAGCCTCTTAGCTTGTTTACCTGGGGGTGCATTTATTTTTGCCTA
ATTTTAACAGGACAGTTTTGCTAAATACAGAATTCTCAGTTGACAAGTATTTTTCTTTTTCTTTTAGCACC
TTAAATATATCATCTCTGTGCCTTCTGGCCTG

The following amino acid sequence <SEQ ID NO. 198> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 70:

FFSHFLNYYFPLFLVHFLHILITFLFPFVYILWIFSLWLPWRLHVTVQSYNNLFINTNLTSIAPNTLLFYN
FPFLLCYVISVKNQSLYMLCTYHGFIIIFVNLPFKFFKKSVVTSQNYIKLLVFIMSMYLPLPEIFIFSYVF
KLLSIVILFQLRAVLTLIIVEDCSLLACLPGGAFIFAFQDSFAKYRILSQVFFFFFHLKYIISVPSGL

The following DNA sequence Seq-2529 <SEQ ID NO. 71> was identified in *H. sapiens*:

TTCTTATCTCTAAAATGAGAATGATGCTGGCTCTCCCACTCTCATAGGGCTGTTATAAAAACCAAATGAGG
ATTGTGCTTTGGAAAATGCTTGCAAAAGATCAAGTGCTACATGTGTGTAAAATAATTTTCCAGGAATATCC
CCAAAGTTTTTGGGCTGGTATATCATATAATTTCTTTCAGTAATTGTGTGGAAAAATACTTTATAAATGCA
TAGATATAGATAGATATTTTCATATAATACATGCAGTGATGATCTGATGAGAAAAATGATGTACCCTGAAT
GTTTTATCTTTTAATAGCACTGGCAATCTTGATATGCATGAATCTTTTAAAACCATGCTACAAACCTCTGT
TTCATTTAGAATATTATGTCTTTTTTGACTTACCCCAAACCCCAAAATGACCAAATGGGAATGAAATATGC
CAGCATGCACCTCATGCCTGGGAAGATACATAAAACAATGGGTTGAGGATTGGATTAAAGAAAGACAAAAG
GCCTTCACACAAGTGATTCTTCCTAAAATTGAAAGGTTACCAGCTAACAAGATAGGAAGGTAGTCTCTTTG
ACCTTCTGCTATTCAGAGAGATATTGGCAATAAACAATTATATGTGTGTGTAGTGTGTGTGTGTGTGT

The following amino acid sequence <SEQ ID NO. 199> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 71:

LISKMRMMLALPLSGCYKNQMRIVLWKMLAKDQVLHVCKIIFQEYPQSFWAGISYNFFQLCGKILYKCIDI
DRYFHIIHAVMIEKCTLNVLSFNSTGNLDMHESFKTMLQTSVSFRILCLFLTPNPKMTKWENMPACTSCLG
RYIKQWVEDWIKERQKAFTQVILPKIERLPANKIGRSLPSAIQRDIGNKQLYVCVVCVCV

The following DNA sequence Seq-2530 <SEQ ID NO. 72> was identified in *H. sapiens*:

CATTTGATTGTGATATGGCTTTTTTGCTTAACACCATAACCCCAGGGCCCGACATAAATTAATGAATTAGT
TAAGCCTGTTAAGTCCTCTGTGCATCCTTCCTCCTATTATATTAACCCCCTCCTCACCCCTAGACTTTTAT
TGCTCAGTGCATATTAAAATCTTCTGATTAGGTTCTAAAACACAATTACATCCCACACTTTAGTGCAGATA
TCTTTCCATGTTCTTCAGTTTGTTTCCAACAGCAAATTTCTAGATTCTCCACATAGATCTTACATTTTTTC
CCCACTCATTAACCAAACTGCATGACTCACAGCCCCAAACATCCCCTAACTATTACATTAGATAACCACCC
TCTCTCAGTTTCAACTGCCTATGTGTTTCTCTGCCCACTAGAATTATACCAAGTATTAAAATCAGCGTAAA
TTGTCACTTTTTTCAGGTAACTTTCTTATTCTTGTTCTACCTGAAAATGCAGTTCTTTCATTCTGCTTCCT
TGGCACTACAACCACACCTCTTTTATGGCATGCATTATATTGAGTTTGTTATACTTCTGCAAATACTTACT
TCAGCTCAAATTCTGTTTGAAGTCACGAATTCGGCTAGTATTTACCTCTGTGTCAATGGCATCCTGCTGGA
AAGTAGATGCAGGCTTGGG

The following amino acid sequence <SEQ ID NO. 200> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 72:

ILYGFFAHHNPRARHKLMNLSLLSPLCILPPIILTPSSPLDFYCSVHIKIFLGSKTQLHPTLCRYLSMFFS
LFPTANFILHIDLTFFPHSLTKLHDSQPQTSPNYYIRPPSLSFNCLCVSLPTRIIPSIKISVNCHFFQVTF
LFLFYLKMQFFHSASLALQPHLFYGMHYIEFVILLQILTSAQILFEVTNSASIYLCVNGILLESRCRLG

The following DNA sequence Seq-2531 <SEQ ID NO. 73> was identified in *H. sapiens*:

ACCTCCCCCTCCCCCAACCAACTGAGAAGCTGCTCCCTCCCCCAGCAAGCCCAGCGCCAGGTGCTCTTGCC
TTTTCCCACTGAGAGAAGGCTGCTCTTTTGTACTGCCCCCCGCTCATTAAACAGCCTCCCCCAGCCCTGAG
TGCACTGATGTCCGCAGCGCTGCCCTACTGTGTCAGTGTGTGTGGGAGTGCCAGGCACAGCACCATCCCCC
AGTTTGGGCCGACTGGGGAGGGCCTGGGGCCCGCCAGGAGACACCTGTGGGAGGCCTGAGAGATGGCTGTA
CCTTGGAGATGGCCTGGTGGAGGACAGACCCCACCAGCCAGCTAGGAGGGGATCTGGGGTCCTGTTCTGGG
GAGGGAAGAGCAGACTCCACGATATCCTTGGGGTCTCCAGATAGCCCACC

The following amino acid sequence <SEQ ID NO. 201> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 73:

TSPSPNQLRSCSLPQQAQRQVLLPFPTERRLLFCTAPRSLNSLPQPVHCPQRCPTVSVCVGVPGTAPSPSL
GRLGRAWGPPGDTCGRPERWLYLGDGLVEDRPHQPARRGSGVLFWGGKSRLHDILGVSRPT

The following DNA sequence Seq-2532 <SEQ ID NO. 74> was identified in *H. sapiens*:

AGTAGACAAATTTATAAAATTATTTTAGAGCAATGAATAAAATAAATAGTATTACTTTTATATTATGTCCT
CAGTTTTTTCAAGTCAATTATTTATTAGCATTTGACTATTATTTTGTAAGCCATAAAATATGCTATGAGTC
CATGTACAGAATATTATCAGACTGGTTGTGTTATTGCAATCAGAGATGTGTAGACCATCCCGTGCAGTGTT
GGCAGGACATCCCGTACATCATGAATTTCCACTCCCCTCTGCTTGCTGTGTGTGGGTTAACTAATAAATAC
TCCATCTTAATCTTGCAAGCCATTTGATAAAGGCATTTTGCAGAATGTCATCTGTCAATTCTTTCCAAAAT
CCTCTAATTCTTCCTTGAAAGTGACCACTAAAAATTTCGGAAGATTACTAAAATGAAGTTGATTGTATTTG
TCTTGCCAAAATAATTGTGTCTATCATGTTTACTTAAGCAAATTACAGAGAAAAATGAAGCGTATATTTAA
TGAAAGAAGTTTCAGAATCAGATTTGTCCAAGAAAGGTGACTTTGTTTCTTTCAATTATCTTAAAAATCCA
ATCCTGAATTTCTAGTAAATTAATTTTAATTGATGTTTGATTCAAGCTTTTAAGACTAAATAATTATATAC
AGCTTTCTGAATTAGATAGTA

The following amino acid sequence <SEQ ID NO. 202> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 74:

TNLNYFRAMNKINSITFILCPQFFQVNYLLAFDYYFVSHKICYESMYRILSDWLCYCNQRCVDHPVQCWQD
IPYIMNFHSPLLAVCGLTNKYSILILQAIRHFAECHLSILSKILFFLESDHKFRKITKMKLIVFVLPKLCL
SCLLKQITEKNEAYIKKFQNQICPRKVTLFLSIILKIQSISSKLILIDVFKLLRLNNYIQLSELDS

The following DNA sequence Seq-2533 <SEQ ID NO. 75> was identified in *H. sapiens*:

ATATGAGAGAATACAATATCAATGTTCACAGTACACACAGATAGTGAAGTAATGTAAATAGCATTGTCGGG
AAAAGCCAGAAGCCAAAATTTTGTTATATAGATAGAGAAATATTATGCAAATCCTGGAAATATCTGACAGA
TGCCCTGCTTGAAGGATAAGCTTATTAGAAAATAAATTACAACTACTAAAGAACAACAAATGTTTCTTGGT
TTTTGGATAGTATGGATTGGTACAGAGAGGTCAATGAACTGTGTGGTGGCACAGATGGTCTAAGACCTACC
CTGGCTCCT

The following amino acid sequence <SEQ ID NO. 203> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 75:

EPGVLDHLCHHTVHPLCTNPYYPKTKKHLLFFSSCNLFSNKLILQAGHLSDISRICIIFLYLYNKILASGF
SRQCYLHYFTICVYCEHYCILSY

The following DNA sequence Seq-2534 <SEQ ID NO. 76> was identified in *H. sapiens*:

ACAGTGCCAAATAATCATCTTTGACAAGCCTTGCTCTGTCAGTTTTAGGCAAATTAGCAAATTCAAATAGA

TGGCAACTGCGCCTTGTCTTTCCAGCTATGGTGATTCTCAGGCTCAGTGTGATACTTTTAACTGCTTGCCT
GATCAAAATGCCTGAAAGCTATGTCCATGTCTCTAGAGTATCATTAAAAGGAAATGGAAGCTTATCCACTG
GTGCCTGCCAATCTTTCCCATCACATGCTATGTTTGATTGACATGTGACACTCTCCTTCATAGTACGTGGG
GAGCCCAGAACTAGCCTGTGGTCCTTAAAGGAAATGTAAAGAGCCCAAGTCATTTTAAAAAGAAGTTATTT
TTCTAAAGGAAAGAGCCTGCTATTTGCTCACTCTTCTCACCTTATGATCCTGAAATACTTTGTGTTAGATA
GCTTCCGAAACTTTTGAGTTACTGTTGGAGAAATAGCAACCTATGTTTCCTCTGTGTTAGA

The following amino acid sequence <SEQ ID NO. 204> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 76:

SAKSSLTSLALSVLGKLANSNRWQLRLVFPAMVILRLSVILLTACLIKMPESYVHVSRVSLKGNGSLSTGA
CQSFPSHAMFDHVTLSFIVRGEPRTSLWSLKEMRAQVILKRSYFSKGKSLLFAHSSHLMILKYFVLDSFRN
FVTVGEIATYVSSVL

The following DNA sequence Seq-2535 <SEQ ID NO. 77> was identified in *H. sapiens*:

TTCCTCTTTTGTCTTGGGTAAGAATAGCTTTTGAGATAAGAATACATTTATTTTTATTACCTTTGTTGATT
CCATCATTTTGTTATTCAGTTATTGTGTACTTTTTATCATAAAAGACTTTGGGGAGAGCTTTGCAGCTTCT
GTTAAATCATGAAACTAGTTTTAATTTAAGCTCAGTCCAAATACAATTTCTCAAAATAGAGATGTTTCTAC
CAACATATCATTTTTATTTCTTGTGTGTAGTCAAAATAAAAAGATTAGACAAATTTGATATAACAGTCATG
ATCACAGGTAAACATTAGAAAGGAATAAACTTTGCTTTTTCACTTGAAAATCCAAGTGTTTTCTTCACATG
AATTGTAAGAAGATAAAACTATACTGACTTAAGGAGGGAGGCTAATGAGAATTTTTTAGCCCATACATGGG
CCTCCTTTAAACTATTTTACTTTTAGTTGTCCTACATTATAGAAAGCTACCAGAAGATTTAGTTTATGCAT
ATACAATTAAAATACAAATACAAATATATGTATGTCTGTGTCTCTACATAGACCTACATTTATTAGTCAAA
CAATAAAAGAAAATTTGTTCCAGTTATAAAATGCTCAAGCCAAATTTGTCACACAGTCAAGGGCTTACTTT
GTTCTTTGAATCATC

The following amino acid sequence <SEQ ID NO. 205> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 77:

PLLSWVRIAFEIRIHLFLLPLLIPSFCYSVIVYFLSKTLGRALQLLLNHETSFNLSSVQIQFLKIEMFLPT
YHFYFLCVVKIKRLDKFDITVMITGKHKGINFAFSLENPSVFFTIVRRNYTDLRREANENFLAHTWASFKL
FYFLSYIIESYQKIFMHIQLKYKYKYMYVCVSTTYIYSNNKRKFVPVIKCSSQICHTVKGLLCSLNH

The following DNA sequence Seq-2536 <SEQ ID NO. 78> was identified in *H. sapiens*:

GTGCTGAATTTGTTCTAATATTATTGGTTACTTGTATTCTACTGTGATGTGTCTCTTCATACCCTCTGACA
TTTTTTCTGTAATACTTTTGGTCTTTTTCTTATTGATCTGTAGTTCTTGAATTAAGGGTCTCGATAATTTT
ATCTGCTGTATGCGTTATAAATAGGTTTTTCACATTGCTGTTTGCCATTCAATTTGATCTTATGGATTTTT
TTAAGTATTCGGAAGCCCTTTGCAGTCAAATGTTTAATTCTCCCTTTTGGTTTTTGCTGTGAACAAACATC
ACACTTAAAAGTCCTTTCCCTTTCCTGAGTTATACATATATGCCTGTATTTTCTTCTAGGACTTTTCTTTC
ACTTTAAAACCTTATTTGATTTGGGATTACTTTTTGTGTGTGGTGAAAGGCAGGACCCTGATCTGATTCTT
TTTCAAGGGGTTTCCTGTTTGTCCCAAGATCATTTCTTAAACAGTCCCGATCCTTTGCTTGATTCTCATCT
GGCGTACCTCATCTGTACGCTGCCTGCCAATATT

The following amino acid sequence <SEQ ID NO. 206> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 78:

VLNLFYYWLLVFYCDVSLHTLHFFCNTFGLFLIDLFLNGSRFYLLYALIGFSHCCLPFNLILWIFLSIRKP
FAVKCLILPFGFCCEQTSHLKVLSLSVIHICLYFLLGLFFHFKTLFDLGLLFVCGERQDPDLILFQGVSCL
SQDHFLNSPDPLLDSHLAYLICTLPANI

The following DNA sequence Seq-2537 <SEQ ID NO. 79> was identified in *H. sapiens*:

ACCTATCATGAAAAACAAAATATCCCACGATAAAAACTAGGAACAAGCTCTGTGTAAAAATGTTTTGTGAT
GCGTGTATTCATCTCACAGACTTAAACCTTTTCTTTGACTCAGCATGCTAAAAACACTCTTTTTGTAGAAT
CTACAAAGGGACATTTTGGAGTGCATTAAGGCCTATAACGAAAAACCTAATATCCTGTGATAAAAACGAGA
AACAAGCTCTCAGTGAAAATGCTTTGTGATGTATCAATTTATCTCTAAATGTTACGCCTTTTTTTTGATTC
AGCAGCTTAGAAACGCTTTGTGTAGAATCTACAAAAAGACGTTTCAGAGCCCATTGTGGCCTATAGTGAAA
AACTGAATACCCCAGGATTAAAATTAGAAAAATATTATCTGTGAAAACACTTTGTGATACATGGATTTATC
TCACAGAGTTAAAACTTTGTTTTGACACAGCAGGTTGGAAACCCTCTTTTTGTAGAATCTACAAATGGGCA

TTTCAGAACACATTGAGGCCTATAGTAAAAAACAAAATATCCCACAATGAAAACTAGGAAACAAGCTATCT
GTGAAAATGCTTTGTGATGTGTGGATTCATCTCAGTGAGTTAAACCTCTGTTATAATTCAG

The following amino acid sequence <SEQ ID NO. 207> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 79:

LNYNRGLTHDESTHHKAFSQIACFLVFIVGYFVFYYRPQCVLKCPFVDSTKRGFPTCCVKTKFLCEINPCI
TKCFHRYFSNFNPGVFSFSLATMGSETSFCRFYTKRFAAESKKRRNIRIDTSQSIFTESLFLVFITGYVFR
YRPCTPKCPFVDSTKRVFLACVKEKVVCEMNTRITKHFYTELVPSFYRGIFCFS

The following DNA sequence Seq-2538 SEQ ID NO. 80> was identified in *H. sapiens*:
ACATTGGGTCAGGATCTTTCTGATGTGTCAATTCTGTCCTCAGACTGGTTTTCTTCCATAAGATGTGCACT
AGCAGTGACTTGGGCAGCATACTTTCATGTTCCTATCTTGCATGAGATAAAAAGACAGAGGATCAGAGAAA
GAAACACAGAGAATCTCTCCCATCACAATGAAACAGAAGTTCCTCTGGAACTTCTTAGGTCAGTTTAGCTG
AAGAGCCCACCAAGTCTTGATTACCATAATCCTGAACCATTAAAACCAATCTCTAGCCAAAAAGATGGTAG
TACTATCAGCCTTCCATGGGTTCAGCATCCATGGATTCAACCAACCAGGGATCAAAAATATTCAGGAAAAG
AAGTGTGTCTATACTGAACATGTACAGGCTTTTTTTTTTTTCTTGATTCCCGAGACAATACAGTATAATA
ACTACTTACATAACATTTACATTGTATTAGGTGTTGTAAGTAATCTGGAGGTGATTTAAAGTGTACAGATG
TTTGGGGGGTTATATACAAATACTATGCCAT

The following amino acid sequence <SEQ ID NO. 208> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 80:

IGSGSFCVNSVLRLVFFHKMCTSSDLGSILSCSYLADKKTEDQRKKHRESLPSQNRSSSGTSVSLAEEPTK
SLPSTIKTNLPKRWYYQPSMGSASMDSTNQGSKIFRKRSVSILNMYRLFFFFLIPETIQYNNYLHNIYIVL
GVVSNLEVISVQMFGGYIQILCH

The following DNA sequence Seq-2539 <SEQ ID NO. 81> was identified in *H. sapiens*:

AGGTGAGCACCAAGTTCTTACACGTGGGAGCAGGATTTGCCTCACATCTGTGCAGGGAGAGCAATTCTTGT
TAACCACCTTAGGGTTAACCTTCTTCTACTCCTTCCATTAACTCAGCTTAGGTCATTATCTCTATGTATTA
AGAATCTGTGCACATGATACACACACTTCACAGGTGTTACATAAAAGAAAACAGAGACTTAGTCTCAACTC
CATCACATATTTATTAATTCATGCAGCAAATATTTATTGAAGTCTAATATGTACTAGACACCAGGCCATGT
GCTGGGGATATTATGCTAAACAGGACAGACACAGAAAAACAGTTAACAAGGGGGAGGGAGTCAAACTCAAA
CCCAGTAAATAGATAAGGAAAATAATTACAAATGTTGATAATATCAACAAACAAAGTAAGATGCTGAGCTA
GAAAACAATAGAGAGAGGAACAATGGTTTGGGGTAGAAACATCAGGAAAGCTTATCTATGGAGGTGACATT
TTAGGTCATGTGTTAGCT

The following amino acid sequence <SEQ ID NO. 209> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 81:

ANTPKMSPPISFPDVSTPNHCSSLYCFLAQHLTLFVDIINICNYFPYLFTGFEFDSLPLVNCFSVSVLFSI
ISPAHGLVSSTYTSINICCMNICDGVETKSLFSFMHLSVCIMCTDSYIEIMTAELMEGVEEGPGGQELLSL
HRCEANPAPTCKNLVLT

The following DNA sequence Seq-2540 <SEQ ID NO. 82> was identified in *H. sapiens*:

GCCTAGGGCGCCCAACTCAGCTCTCTGCAAGGGGAGTCCAGTGACAGAAACGAATAAAGCCATTTTGCTTT
CATTGCTCAACCCAGCACGTTGAGGTGTCCCCAGAACCCCAGTGTACATGGCAAAGATGTGAGGAAAAATG
ACGTTAGGGTATTGTCACCATGTAGTGGGGGAAATTCAACACTGGATGAAGGACTCATCCAATGTGCGTGG
TTAGGTTTAAGCCGGGTCATCTGATGTTTACAGGAGGTAAAGCAGAGCCGCTGGAAGACTTCTCTGACCAG
CAAGGAAGCCATGTGGAAAGTACAGGAGGACCCTGGGAGTTTGGGGAACAAAAGGAGGCCGGGAGGGCCTG
GTGGACCCAATGACCCCTCAGGGCTCGGGACCGCTAGGCCCGAGGGGTGGGGTCACCCTACCTTTCTTTAT
GGCTGTGGTGCTCCTCCATGGAAACCCCAGCTCTGACCACAGGGTGAATGCCT

The following amino acid sequence <SEQ ID NO. 210> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 82:

GIHPVVRAGVSMEEHHSHKERGDPTPRARSRALRGHWVHQALPASFCSPNSQGPPVLSTWLPCWSEKSSSG
SALPPVNIRPGLNLTTHIGVLHPVLNFPHYMVTIPRHFSSHLCHVHWGSGDTSTCWVEQKQNGFIRFCHWT
PLAESVGRPR

The following DNA sequence Seq-2541 <SEQ ID NO. 83> was identified in *H. sapiens*:

TATTATGGACCTGGGGAGGGGCCAGGCCTGGGGCAGGGGGCTTTCTCTGATTATGGCGGCTGACGTAGCCC
ACCCCACTGTGATGTTCCCACTAGCATGGAAGTCCCGAGTCCCTTCCTTCTCCGCCTGGCCAGGTGTGGCT
TCTGGGCAGGCTCCGACCTCTGCGTGCCCTTGGTCTGGAAGCCAGCCCGGGAGCAAGCGGTGAGGTTTGGC
CAGCCCCGTCCTGGGCCGGCGAGGTACCTGCCAGACTGACCTAGTAAAGGGGCCAGGCCCGAGGAACTCCC
TCCCTCGCTCCCTTCTGTCTTTGCCTTCTGCCCGCTCTCCCTCGTCCCTTTTCTCCGCCTTTTCCGCGCTC
CATCTTGCCCTCCTCCCTCCTTCGCCCCCGCTCCTACTCTCCCCTTCTTCCCCTCTCTCCCTACCCCCTCC
CTTTCTGGGGCAGGCGTTTCTCCGAGGCGCACTGAGGCTCCGGGGCGAGTCCGCGCAGCGCGAGCTGGGGA
AAG

The following amino acid sequence <SEQ ID NO. 211> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 83:

FPSSRCADSPRSLSAPRRNACPRKGGGRERGEEGESRSGGEGGRRARWSAEKAEKRDEGERAEGKDRRERG
REFLGPGPFTRSVWQVPRRPRTGLAKPHRLLPGWLPDQGHAEVGACPEATPGQAEKEGTRDFHASGNITVG
WATSAAIIRESPLPQAWPLPRSII

The following DNA sequence Seq-2542 <SEQ ID NO. 84> was identified in *H. sapiens*:

AAATACAGGGATACATAAAGGAACCTCAATCCCTGAGGCACACATTGTCAGTAACATATTAGCAATGGGAG
ACAGGGTGTCATAGAAACAAAGGGCTGGAAAGCATTATTTTTCTGATGTCCCTGGGTATGATTTACTGACT
GGTTTTGCCCTGAGCAAGTACTAAGTACAAAGATTTTTGTTGCAATACATGGAAAAATTCAGCAATTGTGT
TATGATTGTTGCTATTTACTTTATTGTTATTGCTTCATATGAAGTAGCCTGTGAATAGATCTAAAAATTTT
ATAGCATTTGATGGTGAAGTTGGATTTTCTGTTCTGTCAATTTTACTTGAATAATCTGCTTCATTACATTC
AGGGTAAAATACATAGCTGAAAAATAAACCGACGAAGAGAATAAGGGTAATATGCACAGTCTTAAAGCTCT
GTCAAACTCTCAACCCCTAAAGTAACTGTTGGTGCTAGCCAGGATTTCTTCAAAAACCAAAAGCACTGCTT
ATGTTCAAAACACTTGACATCTTCGGAACTCGCATATAAGGTACACCACATGCAAGAGTCACTTTTACACA
TAAAGTTTATAATAATGATTTGGTTCATATTTGGTTACAGTGACAGATACTCTTTTTTCATAAACCCTGTG
GGAAGACCAAAATCCATCTCCGTAGTTTTGCAGTGCCTCTACTGCTGACTTTCTCCATAAATATTTTAACT
GTGCACGTTTCT

The following amino acid sequence <SEQ ID NO. 212> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 84:

KYRDTRNLNPGTHCQHISNGRQGVIETKGWKALFFCPWVFTDWFCPEQVLSTKIFVAIHGKIQQLCYDCCY
LLYCYCFISSLIDLKILHLMVKLDFLFCQFYLNNLLHYIQGKIHSKINRRREGYAQSSSVKLSTPKVTVGA
SQDFFKNQKHCLCSKHLTSSELAYKVHHMQESLLHIKFIIMIWFIFGYSDRYSFFINPVGRPKSISVVLQC
LYCLSPIFLCTF

The following DNA sequence Seq-2543 <SEQ ID NO. 85> was identified in *H. sapiens*:

GGAGATTAGCAGCAATTAAGAGAAGAAATTCCCATTCATATGAGTGATAAAGCAATTAAGTAGAATAACTT
AGAAAAGGTTCTTGGAGAGTCACAGGACAAAATAGCATAGGTACGGTTTCTCTTAATTGAGCTGTTATAAT
TTACAAAGCAGTAGAAACAAATACATGAAAAAAGTATGTGTAACTTCAATAGAGTTTTTATTTTGAATGCA
GAAATCTTCAATGAAATTGAATATGCCTCACCATTTCTAGCTTTATTCTTATCCCAAAATATCAACCACAG
ATGCATAGGCTCCAGGGAATCTTTTGCCTGACTAGAAAACCTTATTTAAGAAACCAGTACCTCTAAACACA
TATCCTTGGGCGATTAGTCTCCTGTGAAACAACTGTTATTTCTACACATCTATTTAGAATAAACTTGGATG
ATTGACTTTTGGAATGTTCTCATTTTTAGAATAATAGAGATGTAGGAAAAAGTGAAAATGCTCTGTCTGTA
TCTATTTAAAGTCTCGACAGCATTAAAGAAATTTATTCTCTTCCTGCAATCACTCAAATCTGAGCACAAAA
CTGAAATAGCATCGTAAACTGACAAAGCTCAAGGGTAAA

The following amino acid sequence <SEQ ID NO. 213> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 85:

YPALSVYDAISVLCSDLSDCRKRINFFNAVETLNRYRQSIFTFSYISIILKMRTFQKSIIQVYSKMCRNNS
CFTGDSPKDMCLEVLVSIRFSSQAKDSLEPMHLWLIFWDKNKARNGEAYSISLKISAFKIKTLLKLHILFS
CICFYCFVNYNSSIKRNRTYAILSCDSPRTFSKLFYLIALSLIMGISSLNCCS

The following DNA sequence Seq-2544 <SEQ ID NO. 86> was identified in

H. sapiens:

TTAAAGGACAGGAAAAAGAAATGCCATGTGAACACTAATCAATATAAAGCTGGAATAATTTTGCTAAAGCG
GACAAAACACTTCAAGGCAAGGAAGTATTACCCATTCTGTGTCAACCTCATTTTTTATATCATTATTCATC
TCTCATATGTGTCTATCTGGTATCCCCAGCCATAATCTGGTAACCTATCTCATCACACGCCTTTCTACCCA
GTGTTTTGCCCACAGGAAATGCTCAGTATATGCCAGTAGTCCTGGGTGTCTCTGCAGATAAGTTGTGTATT
ATCAAAATGCCTGACTTTATTCTCTGTTCAAAGCTTCTCTGTATCATGTGGGTATGATTTTGAAAACTGTC
AATGTTAAATGTTTAACATATTCCTCAGACCCACTGCTGAGGAATGTCCTGCGGAGGACAGTCTAGA

The following amino acid sequence <SEQ ID NO. 214> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 86:

RTGKRNAMTLINIKLEFCSGQNTSRQGSITHSVSTSFFISLFISHMCLSGIPSHNLVTYLITRLSTQCFAH
RKCSVYASSPGCLCRVVYYQNALYSLFKASLYHVGMILKTVNVKCLTYSSDPLLRNVLRRTV

The following DNA sequence Seq-2545 <SEQ ID NO. 87> was identified in *H. sapiens*:

TTCATAATTGTGGTAAGGACCTCTAGTCACAGGGACCTGGTTAATATCAGTATGCCTCATGTTATTTGGGA
ATGATGTATTTCAAAAAGTTTATTGTGTAAATAATAGAAAATTGGCTATTTATACCTAATATACTTAATTT
TTAATTGTTTATTGGTTCTTTTAATAAAATGTATTATATACTTTCTTTGAACCTTGTTAGACCTAAAATAG
TTGAACCTTTTTTTGTTTTTGCTTTTGATGACCCAGGGTCATAATTATAAACATTAATTTCTATATTGTAT
CATAATAAAAATATACAGAATTATTGCTGCATAACCATATAACCCTCCAGTTCTGCAGTTTTGTGTTATCT
CTCCTTTACTGCTGTTATGCCCTTGTCTGCTTTTTATAGCTTTCTCAGACCTCCTAATTTTCCTCTTCCAG
TATGCCTATACTTGGGAGATCAGTCATCAAATTTGTTGTGCTTAAAATAAGAACAACTAGGGTTTGAGTAA
GGACCTAGCAGCCTCTTCTGTGAGTAAAGTGTGGGTACTTTAGTGTATGGACTTCAACATGTATTCTGACA
GCTCCTAAACTCCTTCTGTTTAGGTCTCACTGGGCTGTGTAGCTACTTGATGTCACCAGATAACTAACTTC
CTGATAAGTGAAGTGTAACTGGGTTGGAGTTTTGCCTATGTCGACTCCCTGTTCACTGATGCCC

The following amino acid sequence <SEQ ID NO. 215> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 87:

HNCGKDLSQGPGYQYASCYLGMMYFKKFIVIIENWLFIPNILNFLFIGSFNKMYYILSLNLVRPKIVEPFF
VFAFDDPGSLTLISILYHNKNIQNYCCITIPSSSAVLCYLSFTAVMPLSAFYSFLRPPNFPLPVCLYLGDQ
SSNLLCLKEQLGFEGPSSLFCESVGTLVYGLQHVFQLLNSFCLGLTGLCSYLMSPDNLPDKSVTGLEFCLC
RLPVHC

The following DNA sequence Seq-2546 <SEQ ID NO. 88> was identified in *H. sapiens*:

CAACTGATTATACCCCAGGAGGAAAGCGGACAGATGGATTGACATGAATAACGTCATTAGCCTCTTTGCCT
CTGAGAAATTAGAAACAGGGGAGAAAATGCAATAAAGTGTTTACCCATAGACTCCACAACGTTAGGGTCGG
GTAATATTTTGGTTGCTAAAATATTGCCAAAAGATGTATTTACTCTTTATTACATATTCTTCCATTTCTTT
TGTGAACTGGCTATGAATTCCAAAGTGAAATCTATTAGAATTCAATGGATCATCTTGTGACCACACTCAGG
GAATCACAATTATATACACATTTATAGGGTACTGCTCTGCAAACATAAACAACATTGTGACAAGGGACCTG
CAACAAGAAAAAAGGAAGAGATTCTTTAAATGTTCAAAAGGATAAAAATAGAAAAGAGAAAAAATTTTAAT
GACAAAAAGTATACATCCAAGAGAGAAAACAAATGATAAAACAGAATGAAGAGGGAGGGAAGGGGCAACGT
TAAGAGAGGGTCTGATGGGAGATGAGCGATATTTATGGGGCTAATCCTCCCTCTTTTGGGCTCATTATTGC
CTTTCCCCTGTCGCTCCCCAAAGGCTCCCGCCTGGCTTGTGTTCACAGATGCATGTTTATTCTCCCTGCAC
TCAGCTGTCAGAAACTTCATCTGTT

The following amino acid sequence <SEQ ID NO. 216> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 88:

NLYPRRKADRWIDMNNVISLFASEKLETGEKMQSVYPTPQRGRVIFWLLKYCQKMYLLFITYSSISFVNWL
IPKNLLEFNGSSCDHTQGITIIYTFIGYCSANINNIVTRDLQQEKRKRFFKCSKGKKREKILMTKSIHPRE
KTNDKTERGREGATLREGLMGDERYLWGSSLFWAHYCLSPVAPQRLPPGLCSQMHVYSPCTQLSETSSV

The following DNA sequence Seq-2547 <SEQ ID NO. 89> was identified in *H. sapiens*:

ACTCTTCCTTTGTCTCTTTCAGCTTCTGGTGGCTACTGGCAATTCTTGGTGTTCCTTGGCTTGTGGACACA
TCACCCCAATCTCTGCTTCTGTCTTCCCATGGCCATCTTCCCTATGTCTCTGTCTTCTTTCCTGTCTCTTA
TAAGACATCTGTCATTAGATTTAAGGCCCATCCAATCCATGATGATCTCATCTCAAGATCCTTATCTTAAT
TATGTCTACAAAGCAGCTTTTCCAAATAAGGTCACAATCTGAAGTTCTAGGTGAACGTATCTTTGGGGGCA

AGGAGAATGCTATTCAACTTGCTGAAAACAACTTACCTTGTTTTCAGAATACTAAAACATGCTTCAGTATG
CATGTATATAGTTAGGTGGATTTATAGATCATATTATTTAGTTTTAACCAAATTAATCTTCACAAAATACA
CAAGTGGATCAAAAAATTTTAGGCAAAAACACCCCACATATTGAACACAGCAATCGCACAAGCCCAAGAGA
ATAGGGAAATTGAAAGGCTGACTTTTATCCCATCCTCTGTATAAGCTCTTTGTCAGCCATTGAAAACTGCC
ATAATAACATAATCATACCTAAT

The following amino acid sequence <SEQ ID NO. 217> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 89:

SSFVSFSFWWLLAILGVPWLVDTSPQSLLLSSHGHLPYVSVFFPVSYKTSVIRFKAHPIHDDLISRSLSLC
LQSSFSKGHNLKFVNVSLGARRMLFNLLKTTYLVFRILKHASVCMYIVRWIYRSYYLVLTKLIFTKYTSGS
KNFRQKHPTYTQQSHKPKRIGKLKGLLSHPLYKLFVSHKLPHNHT

The following DNA sequence Seq-2548 <SEQ ID NO. 90> was identified in *H. sapiens*:

AGTTGTGTTTGGTTGGTATTTTGGAAAAGATCTGATAGAATTCCTTGATGGACTCATACTTGGGTAATCAT
TGAAGAGCAAGTCACTGTGTTAGGGGCTGGGTGAGATGAGTATACAAAAGTAAAGAGAACCTGACCCTCTG
GCCAAGACCTTCAGAAGCTCAGAGTTCACGTAATTTTCATAAAATTCAAGTGAGTAAGGGTTACAGCAGCA
ATGAGATGTTCTTTTGCTTTCACAACAGATGAGGCCTCCATGAATGGGGAGTAAGAAGAAAAGGTTTCACA
AAGGAGTAGGCCTGTGAGCTGGGCCATGAAGGGTGGGCTCTGATCTATCAAGCAGAGCAGGGGGAAAGCCC
TCAAAGCAGAAAGAGCAAAGCTGCATGGTGTGAAGACTGCATGTGATTCAGGAACCGTGAGCAATGGTAGA
CTCGTGCCAAAGCACAGTGTGTAAGGAAGACAAGGCTGGAAACGTATGCTGAGGTCTGACTGTGAGAGTTT
GAAGCCCCACTGAGAGGTCTGCACGAATTAAGAATTTCAGAGAAACATGATTAGTTCTACAATTGGAAAAA
TAATTCTGGTGCTAAGAACTAGTAAGGTATAAGATAAGCCTAATCACGGAGTGATTTGAAGT

The following amino acid sequence <SEQ ID NO. 218> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 90:

TSNHSVIRLILYLTSSHQNYFSNCRTNHVSLKFLIRADLSVGLQTLTVRPQHTFPALSSLHTVLWHESTIA
HGSITCSLHTMQLCSFCFEGFPPALLDRSEPTLHGPAHRPTPLNLFFLLPIHGGLICCESKRTSHCCCNPY
SLEFYENYVNSELLKVLARGSGSLYFCILISPSPHSDLLFNDYPSMSPSRNSIRSFPKYQPNTT

The following DNA sequence Seq-2550 <SEQ ID NO. 91> was identified in *H. sapiens*:

GTGGCTGTGCGTCTCTGTGCAGAAGAGGCTGCGCGGTCGGCATGGGGCGACTGTCCAGGAATCCCTGGGGC
TCCTGACCGCCACCTCCCAACCCCTGCCAGGCCGGACACCTCGGTCTGGCTGCCAGGGCAGGGGCGGGCCC
TGGCCTGGCTCGCTGGGGCCTGGGGAGCTGCCCGTGCTTCCAGCCCAGTCTCCCCCTGGCTGCTGCCGGCT
GCTGGCCACTCCCACCTCCCAGGCCTGGCGTGAGGCCCACAGCTGCTGTTGCACAACCCTGGTTAATGTGT
GATGGGGGGAGGCCTGGGCCTGGCCCGCCCCTCTGCCAGGGCTTCAGACCCCTGCCCAGCCCCAGTATCTG
AAGGAACCACAGTGGAGCCAAGCCCGCGATGTGGAGAACTCAGGCTTTCAGGAGACCCTGGCCCTGCTCCT
GGCGGCTCCGGGTGGCTTTCAGCTCTC

The following amino acid sequence <SEQ ID NO. 219> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 91:

WLCVSVQKRLRGRHGATVQESLGLLTATSQPLPGRTPRSGCQGRGGPWPGSLGPGELPVLPAQSPPGCCRL
LATPTSQAWREAHSCCCTTLVNVWGEAWAWPAPLPGLQTPAQPQYLKEPQWSQARDVENSGFQETLALLLA
APGGFQL

The following DNA sequence Seq-2551 SEQ ID NO. 92> was identified in *H. sapiens*:

CTTGCTGGCTTTCCTTCTCCTGGGGGCTGCAGTGCTGATTCCCTCTCTGGTTGGCTTAGGCTCCAACCAGC
TGCAATTGTCTGTCTTCCAGAGAAGAGTATAGCTGATGAGCCTGGAGCTCTGGGAGAAAGAGAGCACACAG
AATCTTTCTTGACCATCAGTCCAGCAGAATCCTACATTGGAGCGGCCACACCCTATTTGGTCCTAAGCCAC
TGCCTCTCTTAAGAAGGTTGAGTGTTGGGCCTGCCCCAGGCACATAGTAAGATGTCACCAGTAGCTAAGGC
CCTAGGGCCTGACAGCAGACCTTTC

The following amino acid sequence <SEQ ID NO. 220> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO.92:

LAGFPSPGGCSADSLSGWLRLQPAAIVCLPEKSIADEPGALGEREHTESFLTISPAESYIGAATPYLVLSH

CLSEGVLGLPQAHSKMSPVAKALGPDSRPF

The following DNA sequence Seq-2552 <SEQ ID NO. 93> was identified in *H. sapiens*:

AATGTTTATATTATAAAGTGGAGTAGAAAAATAAAACATTAAAATACTAGAAAATGAAAGTCAATAATGCT
GAGTGTCTTTTTTAATAGCACCAGGTACTGTTTTAAGCACTTTATAAAAAAGATACTATAAAATATATAAG
CCACTGAGGTAAGTAGTTGTAGAGCTGGGAGGAGCTGGGATTTGAACTCAAGTACTCTGATTTCAGAGAAC
CTGCTTTTAATTTTTATGCGATACTACCTCTTCAGTAAGATAGCAACTATTTAAAAACAATACGAAAGCAC
ACCCACATGCACAGCAGTGAAAAAAAACCCATCATGCAGTGTTTTCATCAAGAGCTGCAGTCTATTTCCCC
ACCCCAAAATCCAAGGTGGCCTTGTGACTTGCTTTGAAAATGAAATGCAGTGGAAGGAATTTTGTGTGACT
TTCCAGACTAGGCTGCAAGAGACTTTGCAGATTCCCCTTCCACATTCTTGGAATGCTGCCCTGAGATAGCC
ATGCAAGGAAGATGGTCTACTCTACCAGGGGATGAGAGACCCTGTGGAGGAGAATTAAGGTACCCTTACCC
CAGCCAGAAGCAACAGCCAGACATGTGAGTGGGGCTATCCTGGGCCTTCTCCATTTCAACCAACCCAGCGG
CTGAATGTAGTCACATGAGTGAGTCCAGGTG

The following amino acid sequence <SEQ ID NO. 221> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 93:

TWTHSCDYIQPLGWLKWRRPRIAPLTCLAVASGWGKGTLILLHRVSHPLVETIFLAWLSQGSIPRMWKGNL
QSLLQPSLESHTKFLPLHFIFKASHKATLDFGVGKTAALDENTAWVFFHCCACGCAFVLFLNSCYLTEEVV
SHKNKQVLNQSTVQIPAPPSSTTTYLSGLYILYLFYKVLKTVPGAIKKDTQHYLSFSSILMFYFSTPLYNI
NI

The following DNA sequence Seq-2553 <SEQ ID NO. 94> was identified in *H. sapiens*:

ATTTTAGTGACATCCAATTCATCAATTTTCCCTTGTGGATTATGTGTGTGTCATATACCTGTTTATGCATT
CATGTTCTAGTCTTTCCCCACGGAAAAAGCTACATTCCATTATGGTAGCACACTTTGCTATCTAACTTATT
TGTAAATCACAAGCAGTCTAGAAATTGTGCCTGGCACACACTAATGATCAACAAATTTATGCTGAATGGAA
TAAATAAATGAATAAACACTAATTTATTAGGTAAAAACATTTTAAGTAAGTCTTTTTTCTAACACTGGGGA
ATGATAACAGTAGTAAAAGTGGCATATTAACATTCTGCAAAATGATTTTAAATCCATTATTCTCTTGGGTT
TTCATACATCCCCTGTGGGGAGGACAGTTCAGGTATGATTCTCTTACT

The following amino acid sequence <SEQ ID NO. 222> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 94:

SKRIIPELSSPQGMYENPREWINHFAECYATFTTVIIPQCKKDLLKMFLPNKLVFIHLFIPFSINLLIISV
CQAQFLDCLFTNKLDSKVCYHNGMLFPWGKTRTMHKQVYDTHIIHKGKLMNWMSLK

The following DNA sequence Seq-2554 <SEQ ID NO. 95> was identified in *H. sapiens*:

GCATGTATCCTCATCCTTGGAAAAATAAACTTTCTGAATTAACTGAGGACCTGTCTCAGATTTTTGGAGTT
CACAAGTGTTTTCAGCTCCTTATTCCATTTCCTTCAAAAGAGATGCAATATTATCTTAAAAATCCTCAAAT
AGTTTACCATTCTCAAATACCAACATGAAATTTCACTTTACTACAAAGCCCTCCAATCGCCAGCAGCTCTC
CATCATGCTTAAGTTCACTTCTTTCTATACAACTTTGCCCTATTTCTTCTTCTCTCAATAGAAAGCAAGTC
CTCATTTATCTAATCTGGGCAATTGCTCCATTGGTCTCCCTTCATATTTCTCATATCTTAACAGCCTTTAT
TGTACTATTTTTCTTTTGAGTTTACTAAAAATGGTTCATATTCTGTACCCCATGCAAAAATTCTCCCTTTC
TAGCACAACACACACTAAAATACTTCTTTGTCCTTGGGTTTTCATTTTTAGAAGACTTTTTATACTTCACA
TGTCTCCATTTTCTTATCTGC

The following amino acid sequence <SEQ ID NO. 223> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 95:

HVSSSLEKTFINGPVSDFWSSQVFSAPYSISFKRDAILSKSSNSLPFSNTNMKFHFTTKPSNRQQLSIMLK
FTSFYTTLPYFFFSQKASPHLSNLGNCSIGLPSYFSYLNSLYCTIFLLSLLKMVHILYPMQKFSLSSTTHT
KILLCPWVFIFRRLFILHMSPFSYL

The following DNA sequence Seq-2555 <SEQ ID NO. 96> was identified in *H. sapiens*:

AGGCCTGGAGCCTGGCTGGCCGGGCCATGCTGCTGGAGGTGCAGGGCACACCCGTTCGTGGTGTTAGGGCT
GGCATGCCAAGTGCACTGCGGTTGTCCACCAACTCCTTCCTGGTTTCCCTGATGTGGCCGTGGGGCTGTTC

GCCTTCCCCTTTGCCATCATCATCAGCCTGGGTTCTGCACTGACTTCCACAGCCACCTCTTTCTTGCCTGC
TTCATGCTTGTGCTCACACAGAGCTCCATCTTCAGCCTCCTGTCCATGGCCATCAACAGGTACCTGGCCAG
CCACAGTCGGCTCAGGCATAAAAGTTTAGTCACTGGGACCCAAACAAGAGGGGTTACTGCTGTCCTCTGGG
TCCTTGCCTTTGGCACTGGACTGACCCCATTCCTGGAGTGGAACAGTAAAGACAGTACCTCTAATAACTGC
ATGGAGCCCTGGGATGGAACCATGAATGAAAGCTGCTGCCTTGTGAAGTGTCTCTTTCAGAATGCGGTACC
CATGAGTTACATGGTATATTTCAGTTTTGGGGGGTAAGTCCTGCCCCCACTGCTCGTAATGTGGCTGATCT
CCATCAAGTTCTTCACAGTGACTGCAGGCAGCTTTAGTACACGGAGCTGATGGACCACTCAAGGACCACCC
TCCAGTGGGAGATATACACAGCCAAGTCGCTGGCTGTGATGGTGGGGGATGTTTGCTCTGTGCTCGCTACC
AGTGCGC

The following amino acid sequence <SEQ ID NO. 224> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 96:

RPGAWLAGPCCWRCRAHPFVVLGLACQVHCGCPPTPSWFPCGRGAVRLPLCHHHQPGFCTDFHSHLFLACF
MLVLTQSSIFSLLSMAINRYLASHSRLRHKSLVTGTQTRGVTAVLWVLAFGTGLTPFLEWNSKDSTSNNCM
EPWDGTMNESCCLVKCLFQNAVPMSYMVYFSFGGVLPPLLVMWLISIKFFTVTAGSFSTRSWTTQGPPSSG
RYTQPSRWLWWGMFALCSLPVR

The following DNA sequence Seq-2556 SEQ ID NO. 97> was identified in *H. sapiens*:

TATTCAGAAACTAGGGTTCATGACGGTGCTTCTGTTGTTACCTAGTAGAAGTAGCTTTGTAAGCACAAAGA
TTGTAGTTTTGTGAAGCTATCTAGTACAGAGTCACTCTGGAAGTTTAGCATTATAGAGTTTTTTCATAGAA
AGGATGGATAGATACAAGTTTTTCCTAACAAGCACAAGTGGCAGTCTTTGAAAACTAATTTTTTATGTGTA
CATTGTAGCATTGGAAGATAACTGTGGTTGAGTGTGATAAACTGAAACTTTTTAAAAAATCTATTATTTTT
TTTACAAGTTAAGTTAGAGCCAGATATGCTGATTCTCTACCATTTTCAAAAGAGGAATTGGAAAAGGGAGA
GCTTGTTTATGTGGTATTCACAATAGTGTCTGCTCCTGAAGAAAATTTTTGGAAAAATCTCATGAGTGTCC
TCAGACTGAAAACAGGGATCCAGTCTGTTGTTCATGCAGGACTCAGGAGGCGAGCGAGCATGTGATACCAG
GAAGGGTCCCATCCCTGCCCTGCTGGGGAGCCCTCAGTGGCGAGGTGGCGAGTTCAGGCTTCACTTCAGAG
CATGGATACTGCTGCATAGGTGCTGGAAGGGTGCTGCATGGGTGCTGGAAGCTGCTTGGCATAGTGCATGT
CCTGTTTCCTG

The following amino acid sequence <SEQ ID NO.225> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 97:

QETGHALCQAASSTHAAPFQHLCSSIHALKSLNSPPRHGLPSRAGMGPFLVSHARSPPESCMNNRLDPCFQ
SEDTHEIFPKIFFRSRHYCEYHINKLSLFQFLFKWRISISGSNLTCKKNNRFFKKFQFITLNHSYLPMLQC
THKKLVFKDCHLCLLGKTCIYPSFLKNSIMLNFQSDSVLDSFTKLQSLCLQSYFYVTTEAPSTLVSE

The following DNA sequence Seq-2557 <SEQ ID NO. 98> was identified in *H. sapiens*:

CTGTAATAGTTAGCCTGATAAGCGGAAAAGGGAAATGTAAGACTCAAATTATTGGTTCATAAAATAAAGCT
CCAGACAATTCTGTTTTATTATACAGAATGGATTGGTTGTGGTCTGTTAGCAGGCAGAGACACTATGCATA
CAGATACCATAATAATAGTAAAGAATGGTTGAGTGGAGAACCAGTGCCTCTGTTCCAATTATTTTTATAAT
TGCTCTCTATCTACTATCTCTACAGATATTCCATAAACAGTGTGCAACACTAACTCCATCCTTTCGTTGCA
TTTGTTATTATTTTTGCTATAGACAAAATTTTCAACCATGCAGAAACAAAAGTTTAAAACCGTTACATTGT
TCTCTGCATTTACAGGTTTGCAGTAATGTAGGGTAATTAGACATGCTGTTAAATGACCAAATTAAACACAT
CATGTTTTGGTAAAGAAACGAACCCAAGAAGTAGTAAAGATGGTGGGGAATTCCTGAATCCCAAAAGCCTT
CTTAATTTTGACCATTGGACATTCATATATGTGTGTGTGTGTAGTAATTCAAATCAGAAAAACAACCAAAA
GGGGCCAGCTCTCAAAATCCAGGCACTTTAGTGAGACAAAGGC

The following amino acid sequence <SEQ ID NO. 226> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 98:

LCLTKVPGFELAPFGCFSDLNYYTHTHIMSNGQNEGFWDSGIPHHLYYFLGSFLYQNMMCLIWSFNSMSNY
TLLQTCKCREQCNGFKLLFLHGKFCLQKQMQRKDGVSVAHCLWNICRDSRRAIIKIIGTEALVLHSTILYY
YYGICMHSVSACQTTTNPFCIIKQNCLELYFMNQFESYISLFRLSGLLQ

The following DNA sequence Seq-2558 <SEQ ID NO. 99> was identified in *H. sapiens*:

TTTTCTGCAAAAGACCCCTTTATAAATAAGTAAACAGCTACTGGCTCAAATTTCAATTGTATTCTTCCTGG
ATTGTGTTTTTTTAATTATTTTTTCGCTGTTGTCACTGAGCCCTTCCATGTCTCCGAAATTCACACCTTCC

ATGCTTTCACAATAAGAGTCTGGCCAGTCATGGCCCCACAAATTCTATACACCATACCCTTGTTGGTTCAT
TTTATCAACTTATTGGTCTATTTCAAGTCTGTCTTTTACTTGAGAAAGAAGAGAAACTTCTCTGTTTACAA
GGATCATATAGTTTTACCTTATACAAGTACGTAATTTGTCTATATTGTCTATTGTTAATGTATTCATACCA
TTGTACCAAGTAGCCAAGACTGGAAGCAGTCCCCATAGGCCACCCCCACAGTTTGGGAGGGTTGTCAGACA
AAGTTATGGGATACTTAGTCACCACAAAACTCTGGCTTGAAACTTGTCTCCTTCCTCCCCCAAGTTCCTCA
GGAATGTATAGTCACTGTCACTGCTGGGTTTACTTCTGTTATTTTTAAGTGTTTGTGATGTGAGTTTCCTT
AGAAAAGCACCTGACAGTAATCTAGTTCAT

The following amino acid sequence <SEQ ID NO. 227> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO.99:

FSAKDPFINKTATGSNFNCILPGLCFFNYFFAVVTEPFHVSEIHTFHAFTIRVWPVMAPQILYTIPLLVHF
INLLVYFKSVFYLRKKRNFSVYKDHIVLPYTSTFVYIVYCCIHTIVPSSQDWKQSPATPTVWEGCQTKLWD
TSPQNSGLKLVSFLPQVPQECIVTVTAGFTSVIFKCLCEFPKSTQSSS

The following DNA sequence Seq-2559 <SEQ ID NO. 100> was identified in *H. sapiens*:

TTTTATCACCCACAAAACTTTATAATCTGTCACTTGACTCATTGGTTGCCTATTAGCCCATTCCCAAGACA
TACTCCTGAGAGCAGGCCACTGTAAGGTCATACAACCTAAAACAAAGCCACACAAAGAGCCAGAACTTTTATA
TTTAGAAAAAAAAAATGTGCCCAGGATGTATAATTCACATTAAATGCCATTTGTTGAAAGCCAATAAATACA
TATATATGTCTAGTGCACAACTCACAGAAGATATCCTTAATCTACTTATACTGGAAACATACTTACAACAA
AGGATTTTGATGGACATAGCGTGAGTTGTATTTTCAGCTTTAATGAAAGATCTCATGCCAATGACAAAAAG
ATTTCCAAAGCAGGTAATGAAAGCTATAACCCAGACAAATATTCTGAGGATATTGTTAGCCAAGAGGTCCT
CAAATGAAGAAATGCCGTCCGTCAAGGGCATACATATTCGGACATGGGGAGCATAGGAGCAGTATCGAAAG
TTTTTGAAATAACTAAAGTCAAAGGGAAAAAAAGTGTCACTTTGCAGCAATGATACAGAACCTACAGTTGC
AGTCCTAT

The following amino acid sequence <SEQ ID NO. 228> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 100:

RTATVGSVSLLQSDTFFPFDFSYFKNFRYCSYAPHVRICMPLTDGISSFEDLLANNILRIFVWVIAFITCF
GNLFVIGMRSFIKAENTTHAMSIKILCCKYVSSISRLRISSVSCALDIYMYLLAFNKWHLMIIHPGHIFFS
KYKSSGSLWLCFRLYDLTVACSQEYVLGMGATNESSDRLSFVGDK

The following DNA sequence Seq-2560 <SEQ ID NO. 101> was identified in *H. sapiens*:

CAGCACTTATTCCCCGCTGCATGCTGGTGTCTCTCAGGACAGGGGAAGTCTGCTTAGAACTGGCCGGTGCC
AACCTGCACTGGCACTGCTTAGTAGGCCAGTGCCAACCTGGGATTCTCATGGCTGTGTGCTCTGTGCTCAC
CCACCTGTGAATCACCGGGTGGTACAGAGTGACAATCCATCAGCTGTTAAGATAAGATGAATGCAAAAAGG
ATGACATTGCCAAACAGACTGTTGGGTTATTTGGAGGTATCTGTATGACAACTCTAACCCGAAATTTCATA
TTTGGCACAGCCATGGCCTGTGGGGATGGCTGGCATTCTGGATATGTTGGAAACAGCACTGGTTAGACATG
GAGCAATGTCCAAGTGCCAGCCCCACTCATCTGCTACACGTGCTGTGCTATTCTGCTTCACTCGCACAAAA
CTAGACTGCAGCGCAATATACCGGCTCATCCTTGTGTGGTTCTCCAGCACTCACGGGCAATTATTTCTCCA
TTTCTATGTGTTTTAAACCTGTTTTCTCTCCGACCTGTCAATGAGAGCATGAACCTTTATGAACCCCACCT
CCCTGGACCCTCTTGATAGGTTTCGTGGAAGTGGAATCATTCTAAGAAGCAGTGAAGGCAGGGTGCTGTTT
TCTGCTTTCACAGCTCTG

The following amino acid sequence <SEQ ID NO. 229> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 101:

ELKQKTAPCLHCFLEFHFHETYQEGPGRWGSRFMLSLTGRRENRFKTHRNGEIIARECWRTTQGAGILRCS
LVLCESRIAQHVQMSGAGTWTLLHVPVLFPTYPECQPSPQAMAVPNMKFRVRVVIQIPPNNPTVCLAMSSF
LHSSYLNSWIVTLYHPVIHRWVSTEHTAMRIPGWHWPTKQCQCRLAPASSKQTSPVLRDTSMQRGISA

The following DNA sequence Seq-2561 <SEQ ID NO. 102> was identified in *H. sapiens*:

AGGTTCCACTCTGTTAGCTGAGTACACACATCACAAACTTGTTTCTCAGCAATCCTTCTGTCTCGTTTTTA
TGGGAAAGATTATACTTTTTCACCGTAGGCATCAAAGCGCTCCAAATGTCCACATCCAGTATACTACAGAA
AGAGTGTTTCAAACCTGCTCTATGAAAGGGAATCTTCAACTCTATGAGTTGAATGCAGACATCAGAAAGAA
ATTTCTGAGAATGCTGCTGTCTACCTTTTATTTGAATTCCCGCTTCCAACGAAATCCTCCAAGCTATCCAA
ATATCCACTTGCAGATTCCACAAAAAGAGTGTTTCAAAACTGCTCTCTATCAATGGCAAAGTTCAACTCTG

TTAGTTGAGGACACATATCACCAACAAGTTTCTGAGAATGCTTCTGTCTATTTTTTATGGGAAGATATTTC
CTTTTTCACCGTAGGCGTCAAGGCGATCGAAATGTCCACTTCCACAAACTACAAAAAGAGTGTTTCAAACC
TGCTCTATGAAAGGCCATGTTCATCTCTATGAGTTGAATGGAAATATCCG

The following amino acid sequence <SEQ ID NO. 230 is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 102:

GSTLLAEYTHHKLVSQQSFCLVFMGKIILFHRRHQSAPNVHIQYTTERVFQTCSMKGNLQLYELNADIRKK
FLRMLLSTFYLNSRFQRNPPSYPNIHLQIPQKECFKTALYQWQSSTLLVEDTYHQQVSENASVYFLWEDIS
FFTVGVKAIEMSTSTNYKKSVSNLLYERPCSSLVEWKYP

The following DNA sequence Seq-2562 <SEQ ID NO. 103> was identified in *H. sapiens*:

GGGAGCGAATTTCAACATGAGTTTTGGTGGGGACAAATAAATCATATCCAAACCACAGCAGCAATATTACA
AATATATAAATGATGACCCAAATATGATACATAAAAAATGCCTTTGTGATCTCAAACACACAGAGGTAGGT
GGAACTAAGCCTGTGGACTCTAGGATCCAGGCTCTGAATCTGTCATTTAGCAGAAGTAGCCTGGAGTTCAA
TTCTTCAAATAACTGGAAGCTGTGATGTCTCTGGAGTGACCTGTCCTGCATCAAGCTGTGTCTTGGAGGTA
GCACAGGGACCTGAGACAACATAGAGTGAACTGCTGGCTCAAGCCCCCTGTTACACTGGGTCTGCAATACT
GCCAAAAACAAGAGAGCCTACATATAAGCCTTGTTTTGAACCAGAGAGCCTGCTGCTTTGGGTGAATGCAG
TTAAGAATAAGCAGACGTGAGAACAGGTGGAGAAACACTCTCTCTCTCTCTCTCTTGCCCTCTCCCTCT
CTCCTACTGAAGATGAGTCTGTATATTAAAATTCTAAAGCACAACAAACAAATATAATGAAAAGTAGCCAA
CAAACTGAACAAGTAGGAAAATTAATTCTTGAAGCACTTCAAATAATAGAGCAAAGCCTGAACTGAACTTA
AATGAAGTATATTTGATTCCTCAGAGATAAAGGTGGTAATAACACCTATAAAGCAAGCATAAGAAATCATG
AGCCAAAAAACAAGAGTCAAAAAGGCTTGGGAAGTTTGGGTGTGGTGGCAGA

The following amino acid sequence <SEQ ID NO. 231> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 103:

CHHTQTSQAFLTLVFWLMISYACFIGVITTFISEESNILHLSSVQALLYYLKCFKNFSYLFSLLATFHYIC
LLCFRILIYRLIFSRREGEGKRERERECFSTCSHVCLFLTAFTQSSRLSGSKQGLYVGSLVFGSIADPVQG
AASSSLYVVSGPCATSKTQLDAGQVTPETSQLPVIRIELQATSAKQIQSLDPRVHRLSSTYLCVFEITKAF
FMYHIWVIIYIFVILLLWFGYDLFVPTKTHVEIRS

The following DNA sequence Seq-2563 <SEQ ID NO. 104> was identified in *H. sapiens*:

AAAATTGGACTCCTGAAGGCACATGTGTGTGTAGTTTGGCAGATTACAGGAAAGCCTTGTAAAATGCTCCC
AGATGTTTGATGCATGAGAGGGAAAATGCCAGGAACAAGGATCAAATTGAGGTGGGTTTCAGACATTATAA
AATCTGTTGATGTAAAAACTAAGAAAACAAATAAGATCATAGGCATGAAATCCTTCTGGAAGGTCAATAAT
GATAAAGTTTTACTATATTAAACCGATTTGCTCCTTTTCTTTTCCCATCTGCCTGAGGCTATTATAAAAAA
ATATTAAGGAACATTATTGCTAATCCATAATAAATGGTACATTAACTATGATCCAACTTATCTTTTCTACA
CAAGGGCCACGGGACTGCATGTGGATAAAATCTGGACTGGATTTATTTTTTTAGGGGCCTGATCCCATGTC
CAATCATTAACCTTTAAGGAGGTTCTTAAAAATAATTTTATTATTAAGAAGTTGAATCATCATAATTATAG
TATCCCTCTGACTTCAAA

The following amino acid sequence <SEQ ID NO. 232> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 104:

FEVRGILLFNFLIIKLFLRTSLKVNDWTWDQAPKKINPVQILSTCSPVALVKRVGSLMYHLLWISNNVPYF
FIIASGRWEKKRSKSVYSKTLSLLTFQKDFMPMILFVFLVFTSTDFIMSETHLNLILVPGIFPLMHQTSGS
ILQGFPVICQTTHTCAFRSPI

The following DNA sequence Seq-2564 <SEQ ID NO. 105> was identified in *H. sapiens*:

AAAAGCATTTCTGAAAATATTGCTTTGAGCAGGATGATAGACTTGTTATAGGGAAGATTCCATTCATTGAA
AGCTTACTTAAAAATATTTCCCTAGTTATATTTTTATTTTTATTAATAGTTTTTTAAATGACATTTATTTC
TGGGTTTTCACACATGTGCTTTACATGTTCTTGTTTTCCTTTACAATTGAACATACACTCTATCAGCCAGA
GGCCAGTGAGCATTTGATGGGGGCCAAAAATAAAAAAAAAACGAGTTTTGGCATAGCTAATACTTTTCATC
TTTGCCTCATCCATATTAAGTTTGAGTCTTGGGCTTATTATTAATTTGAGCACTTTCATT

The following amino acid sequence <SEQ ID NO. 233> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 105:

KAFLKILLAGTCYREDSIHKLTKYFPSYIFIFINSFLNDIYFWVFTHVLYMFLFSFTIEHTLYQPEASEHL
MGAKNKKKTSFGIANTFHLCLIHIKFESWAYYFEHFH

The following DNA sequence Seq-2565 <SEQ ID NO. 106> was identified in *H. sapiens*:

GAATGATACAGCCACTTGGGGAAAAAAAAGGTCTAACAGTTTCTGATAAAACTAAGTCAGTAATTCCACTC
ATAGGTATTCATCTCAGAGTAAGTAAAAGCGGTAGTCCATTAAGAAACTTGGATAAGAAAGTTCACAGTAA
GCTTTATTCAAAAGACCCCAAAACTGATAACAACCCAAATGTTCACCACCCAGAGAATGAATAAACAAATC
ATTCTGCATTCTTAAACAAAACAAAAACAAAACAAAACCACTCCATGGCAAACAAAAGGAGAAAATGCCTG
ATACACACAACAGCATGGGTGAATATCAAGAACATTTGCTGAGTGAAGGTACAGTTATACAGTAGCGCATT
CTGTATGGGTCCACATACACAGAGTTCTAGAATATATAAAAAAAAAACTATTCTAAAAAAGGAAATAAAAA
CAGTTGTATTGTTTGGGGAGGTGGGGA

The following amino acid sequence <SEQ ID NO. 234> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 106:

PTSPNNTTVFISFFRIVFFLYILELCVCGPIQNALLYNCTFTQQMFLIFTHAVVCIRHFLLLFAMEWFCFV
FVLFKNAEFVYSFSGWTFGLLSVLGSFESLLTFLSKFLNGLPLLLTLRIPMSGITDLVLSETVRPFFSPSG
CII

The following DNA sequence Seq-2566 <SEQ ID NO. 107> was identified in *H. sapiens*:

AAAACATAAAACTTTTGAAACTCTTCTAAGAATGTCTAACACAAATTACCTGTATAGATATCATGGCACAG
ACGATGCTGAGGCCGGACTGACTGAAGAAGAACAGGCTGAAGATGCTGTACTCACACAGCAGCTGGCCCCC
AGGTTACCCGCCCTTCATGTACATGGCGATGGTCACCTGGCTCACCAGCAAAGTGAACAACAGGTCGGTGG
CAGCCAGCCGCATAACTGTGTAGAAGGTGGTCTCCTTCTGCTCCTTGCGCGACTTGCACAGCACCACGATG
GCCACCAGGTTGCCCACCACCCCGAAAATGGACGGGTCCCAAGCTGTCCAG

The following amino acid sequence <SEQ ID NO. 235> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 107:

WTAWDPSIFGVVGNLVAIVVLCKSRKEQKETTFYTVMRLAATDLLFTLLVSQVTIAMYMKGGPGGQLLCEY
SIFSLFFFSQSGLSIVCAMISIQVICVRHSKSFKSFMF

The following DNA sequence Seq-2567 SEQ ID NO. 108> was identified in *H. sapiens*:

GCGTCTCTGCCCACCGCTCAAAACTCTAATTCAGCTTCTTTATCTGCAAACAGGAAATGTAAACGTTTTCT
CGAGGAGTCATGAGTTCAAACAGGGTCACCGATAAGGGAGGGTTGGAACTTTCAGAAGAAAATTGCTAAAT
ATGCCAAGGTGTCATATTATTTTTTTCCCAGCATATTAACTAGGGCTTAAGACCTGATAGCCCTGTGAGTA
TGCGTCTGTCTCTTGTAGCAGCGCTGTTCGCTTAACAGAGCCAAATTCAGCCCAGAGTGAGTCTTTGGTGT
CCATCCCAGGCTCTGGCTACCATGTCACCCAGACGGCCTGATTTGAAGGCAGTTTCCTTCCCAGGGACCAC
GGCAGAGTGCCACAAGATTAGCAGAGAGTCTCGTCTCCAGCTTGTTGACGTACGCTACAGGTCTTGGGATT
TGCCAGCATCTTATAATTTTGTACAATAAATGAAGCACCCATGCAGTGCACACACACACGTACACATGCTA
TTAATTCTATGAGTCTTGGGACTTGCCAGTCTCTTTTTTTTTTTTGAGACAGAGTCTCGCTCTGTCACCCA
GGCTG

The following amino acid sequence <SEQ ID NO. 236> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 108:

SLGDRARLCLKKKKETGKSQDSNHVYVCVCTAWVLHLLYKIIRCWQIPRPVAYVNKLETRLSANLVALCRG
PWEGNCLQIRPSGHGSQSLGWTPKTHSGLNLALLSEQRCYKRQTHTHRAIRSALVNMLGKKYDTLAYLAIF
FKFQPSLIGDPVTHDSSRKRLHFLFADKEAELEFAVGRD

The following DNA sequence Seq-2568 <SEQ ID NO. 109> was identified in *H. sapiens*:

AGCACACGGACCACACCCCTAGAAAGAGAGTCAGCATTCACAGACATCAACCTGGCACCACAAAAATTCTT
GGTCCTCAAAGAAAGATAAGATTGTATTTGGTAAACTCTGATTCCTAAATAGGAAAAGGAGCCTGAGACAG
ATTGATAAGATATTAAACAAGGCTGAAAATGAAAAAAAAAAAAAAAAACTTCTGGTGGCCCAGAAGGGTTGA
GTTGATCAAAGTTTGAACTACACACTGTAAATCAAAGTTAATTACATTTTTACTCCAGGTTGTATGTGGTG

GATTTTGTCATCATTTTTACTTGTTCCTCGGTGTTCTCTTTCCCAGTGGAAGCTCCTGGGGGAAAAGGGCC
AAGAGGTTCTAAGTTTCCTCATATGGCCCCTAGCACCACATCAACACAGGAGAGCACATCATAAATACCAT
TTGATGATTTTCTTCCCGCGCATTCATAGCCCCAGACCCTGTGTAAAGGCCTGCTGAGCAATATCATTCAC
TGAAGTGCTACTCTCCCTGCAGGTTGGGTCCAGAAAATATGGTGCTCGGAAAACACTGTAAAAGCTGCCTC
TTTAATAAGGATCCTGGTGTCCCGTGATGGATGCTATAAAACCTCAGACTGGCTGGTGTGCTCACAGCCAT
GTAGGACCATTAACAGCGTCTGGT

The following amino acid sequence <SEQ ID NO. 237> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 109:

STRTTPLERESAFTDINLAPQKFLVLKERDCIWTLIPKEKEPETDDIKQGKKKKKKLLVAQKGVDQSLNYT
LIKVNYIFTPGCMWWILSSFLLVPRCSLSQWKLLGEKGQEVLSFLIWPLAPHQHRRAHHKYHLMIFFPRIH
SPRPCVKACAISFTEVLLSLQVGSRKYGARKTLKLPLGSWCPVMDAIKPQTGWCAHSHVGPLTASG

The following DNA sequence Seq-2569 <SEQ ID NO. 110> was identified in *H. sapiens*:

AAATAGTCCTTAGACTTGTAAATACCTTGACTCGAAGGCAGATAAAGTGAACCAGTATGAAAGCAAAAAGA
CTGGAATCAAAAGCGTTGCTTCTAAAAAAGGAGAAGAAATATGTTCTTGTAATCACATGAGGAGGAAGATA
ATGGGACAAACAACTGGCTTCAGGATTTTTTTTTCTTTTCTGAGATTCACACCAAATTTCTGCATGCTTGA
GATTTACTTTACCTAAAATTTTTAGGCCCAAAATCAGTAGAAACTCAATTGACTGTTTTGGGGGACCTTGT
CTGTCGACAGTGTATTTGATTTAAATGGGACAATATTGTGGAAAAGTCTGCCCTTTACTAGCTGTTCCAAA
TGTCAATTCCATCTGAGCCTTCTTCTATAAGGGGACATTAATGTCTTTTTCTGACATTTTTCCTCATGATT
GACATTCCCAGAAATTTCTCCCCAGCTATTAGCTTCATTAACATTATTATTGCATTTGGTTGGCATTCTTT
CCTCTACCTAATTCTGTAAAGATCAGATAGTATTTGTTCTAGAGATAAACTTTTTCTTTTCTCATACACAC
ACTCAGTACACAAGAAGCCCAC

The following amino acid sequence <SEQ ID NO. 238> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 110:

WASCVLSVCMRKEKVYLNKYYLIFTELGRGKNANQMQCSLGRNFWECQSGKMSEKDINVPLKKAQMELTFG
TASKGQTFPQYCPIIKYTVDRQGPPKQSIEFLLILGLKILGKVNLKHAEIWCESQKRKKNPEASCLSHYLP
PHVITRTYFFSFFRSNAFDSSLFAFILVHFICLRVKVFTSLRTI

The following DNA sequence Seq-2570 <SEQ ID NO. 111> was identified in *H. sapiens*:

AGGATTCACAATGACTGGGTAGTGCAGAGGGCGACAGGATGGCTACAAAGCAGTCATAGGCCATCATGGTC
AGGAGCATGTCTTCTATACATGCAAAAAGGACCAAGAAAGACATCTGTGTCAGGCAGCCCGCATGAGAGAT
GACTCTGCTATGCAACTGCATGTCCACAGTCATCTTGGGAACCGTGGCCGAGGTGAAACTGAGGTTAGCCC
AGCACAGGTTGGAGAGGAAGAAGTACATGGGGGTGTGGAGGTGGGAGTCAGGGTTGACAGCCAGGATGATG
AGCAGGTTCCTCAGCACCGTGACCAGATACATGGACAGGGACAGGGACAGCAAAGCAAGGACCGGCTGCAG
TTCTGGATCCCCTGAGAGTCCCAGGAGGAGGAATTCTCAGACACCTGTGAGACTCCGTGGCTCTGTGTGAC
TTGGACACCTTGAGAAGGAAAGAAGATTGGAAAAATAAAAGACAAAAAGCAGCCCTTCATGCTGAATGCAA
GCAATTCACAAGGGAACATTTTCACACTTGCAGACCATACACCGCCAGCAATGTTTCTCAGTTGTGACAAA
TCCAAAAATCTCAGAATTGTTACATGTTTTACTTTTTTGCTATTCAACTCTTTCTGTACATACTACTTTAG
AGAAAATCCACT

The following amino acid sequence <SEQ ID NO. 239> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 111:

WIFSKVVCTERVEQKSKTCNNSEIFGFVTTEKHCWRCMVCKCENVPLIACIQHEGLLFVFYFSNLLSFSRC
PSHTEPRSLTGVEFLLLGLSGDPELQPVLALLSLSLSMYLVTVLRNLLIILAVNPDSHLHTPMYFFLSNLC
WANLSFTSATVPKMTVDMQLHSRVISHAGCLTQMSFLVLFACIEDMLLTMMAYDCFVAILSPSALPSHCES

The following DNA sequence Seq-2571 <SEQ ID NO. 112> was identified in *H. sapiens*:

ATTTCCCTGATGTTACAAATGAGCAATTGGATGACAGATGGTTAAATATTTTGATACTTGCAGCTAAAAAT
AAAATAAAATCCACCCGAAAAGGACCTTTGTTATCACATACCTACAATTATAGTGGTAGTGTGGTCTCCAT
GATTGTTTGATGTAATAGATCAACAATGTTATCCAGGACCTGGGTTCATGCTTTCTCGCCATTTCGCTATC
TTTAGTTCTGGATTCATATCAAGATGGCTACAGCACTTTCAGCAATCATACCATGCTTGACACTAACTAGG
GAAGAATAGAGAATGTCTCTTTCTTTGAGTCTCTCTTACATCTTATTGGCCAGAACTTGATTATCTGCCCA
TCTCTGAACCAATTATTGTCATGACAAATGAAGTATCCTTGGACAATGAAACACATTGCTGAAACTGGGTT

AGAACTTCCCCCAAGGCACAAAGATAAAGAGGGGAAGGTGAGATAGCTAAACAAATCTGTTTCTAGTATAA
GTGGAAAAGGGGAGAATGGATACTTGGTAGACAAACCATAGTGTCCATTACTAAAAGATACTTGAGGGACA
ATGTACAGTGAATTAAAGTGATACAATTGCTAATGGGTTGAGTAATTACACATTT

The following amino acid sequence <SEQ ID NO. 240> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 112:

MCNYSTHQLYHFNSLYIVPQVSFSNGHYGLSTKYPFSPFPLILETDLFSYLTFPSLSLCLGGSSNPVSAMC
FIVQGYFICHDNNWFRDGQIIKFWPIRCKRDSKKETFSILPLVSSMVLLKVLPSYESRTKDSEMARKHEPR
SWITLLIYYIKQSWRPHYHYNCRYVITKVLFGWILFYFLQVSKYLTICHPIAHLHQGN

The following DNA sequence Seq-2572 <SEQ ID NO. 113> was identified in *H. sapiens*:

GCTTCCAGGGATGCTGACAATGTTGTACTTCTCGACTTGAGTAGTGGTTACATGGGTGTTCGCTTTGTGAT
AAATCATTGAGCTAAATGTGTTTATTTCGTGTACTTTTCTGTATGCATGTTATATCTTACAATTAAGAAGT
TTTAAAAAGAAGACTATTTACTGGCAAGGAAAGCATATTCCTGAAGTATTATGAAATGAAAAAAGTTTACA
AAACCATTTATATGGTGTGATCTCAATTTTACTCTATGAATGTACATATTTATACACATTTATATAAATTA
AATGATCTGGAGTGATAAACATCCAGGTAAAATGGTAGTAATCCCTGGGTGCAAGCACAAGTGTTTTTGTT
TGTTTGTTTTTTAGTGTCTATATATTTCTGATCTTTCTGTAATAAGCCTTTATTGCTTTTCTAATAAGAAA
TAAAGTCATTTTGTAGTATCGACCCAGGAATAAGCCAACAGATCGATAGAACAGAATAGAAAACTGAGAAA
GAGATTCAGTAGATGTAAGAATTTGATGTGTGATAAAGGGGGGGATTTTGAATCAATGGAGAAAAGATGGG
TAGTTCGATACATTTTGGTTAGTTCAATTGGCTAACC

The following amino acid sequence <SEQ ID NO. 241> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 113:

LANTNQNVSNYPSFLHFKIPPFITHQILTSTESLSQFSILFYRSVGLFLGRYYKMTLFLIRKAIKAYYRKI
RNITLKNKQTKTLVLAPRDYYHFTWMFITPDHLIYINVYKYVHSSKIEITPYKWFCKLFSFHNTSGICFPC
QIVFFLKLLNCKIHAYRKVHEINTFSSMIYHKANTHVTTTQVEKYNIVSIPGS

The following DNA sequence Seq-2573 <SEQ ID NO. 114> was identified in *H. sapiens*:
AATACCCCATACTATGGCACCTTGGCAGGCTGAATACTTTGGACTGAAGGAAATTGGAAAGGCCTCAGAAG
CAAGCTCTTTCTGACCTTCTCCCATCCTCCTGTTCCTCTGTCTCCCCTAAATCTAAGTGAGTCTTAAAAAC
CAGAATTCCTCTTCCCCAAGGTAGGTCATAAAAACTTGAACCCCTCTACCCCAAATCAAATCATAAAACCT
ATAAATGTCACACTCTCCCTTCTCCCTTAAGACCCTTATTAGATGCAGGTCCTCCCCTATATCTGGGAAAA
AGGCATCCTTCACAGAGAAATCAAGAAGTATCTGAACAGAGAGGCCTGCTGGTGTCCCCCCTGCTGTGGTT
TGGATATGGTTTGTTTGGCCCCACTGAGTCTTATGTTGAAATTTGATTCCAATGTTGCAAGTGGGGTGTGG
TAAGAGATGTTTGGGCCATGAGGGTGGATCCCTCATGAGTGACTTGGTTCCATTCTCACAGGAGTGAGTTC
TCACTCTTAGCTCCCAAAACAACTGTTTGTTGAAAAGAGCCTGATACCGCCTCCTCTCTCCCTCTTGCTTC
CTGTCCTGGTGTGTGACCTCTGTACACTTCGGGTTCCCTTTGCCTTCTGCCGTGAGTAGAAGCAGCCTGAC
GCTCTTGCCAGAGCAGATGCTAGTGCTATGCTTCTGGCATGGCCAGCAGAACTGTGAGCCACATTTTC

The following amino acid sequence <SEQ ID NO. 242> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 114:

YPILWHLGRLNTLDRKLERPQKQALSDLLPSSCSSVSPKSKVLKTRIPLPQGRSKLEPLYPKSNHKTYKCH
TLPSPLRPLLDAGPPLYLGKRHPSQRNQEVSEQRGLLVSPLLWFGYGLFGPTESYVEIFQCCKWGVVRDVW
AMRVDPSVTWFHSHRSEFSLLAPKTTVCKEPDTASSLPLASCPGVPLYTSGSLCLLPVEAARSCQSRCCYA
SGMASRTVSHIF

The following DNA sequence Seq-2574 <SEQ ID NO. 115> was identified in *H. sapiens*:

AATGTTAATAAAGAAGAACATATGGAGAAAACTCTTGTATTGCAAAACATGAAGCCCATGTGCCTTCATCA
TCCCCAGAAGTCTGTCTGTTCATGCTCCCTGGGATTCCGTTCAGAAAACAAGTAAATGGTGCCTTCTGCAC
ATTTATGTTAAACGGAGAACCAAAAAGAGTGACTACCCCACTCCAGTGCTTGCTGGGGCTGGGAGAACAAA
GAAGCTGCAAGTATGAGGTACTCAAAGACAGTGTTACTAGGGTAATGATTTTCCAGTATGGCCAAAAGACA
TCTTCTATGCAACCAAGCCTCACCTGGCCTTACAAAACAAAAGTGGTTTGGCCAGAGCTTGAATAACAGCT
GGGATGGATGGCCCAATGTAAAGGAGCAGGTGGCAGGCCAGTGGACCCCACTCTGGGGTGGCCCCATGGTG
GACAGAGCCCCTGCTCCCTAAAATGGCCAACACCTGTCCCAAGGAAGGCCACCTAGCCAGAAGTGCCCACC
ATCTGCTGTAATCAAATTTGCAATCACAGGTAACTTTTCCTCTCAAGGGTCCAGCTGGCAATATAAATAAA
TGGAATGAATGGGGCTCCTCAGATGAGTACAGCATCTTCCATGTATGGGGAGCAGACATTACTGAGCTGCT

GCCATGTGGGAATCTCAGTCCAGTTGTGCCAGGTCTTCTGAG

The following amino acid sequence <SEQ ID NO. 243> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 115:

CRRTYGENSCIAKHEAHVPSSSPEVCLFMLPGIPFRKQVNGAFCTFMLNGEPKRVTTPLQCLLGLGEQRSC
KYEVLKDSVTRVMIFQYGQKTSSMQPSLTWPYKTKVVWPELEQLGWMAQCKGAGGRPVDPTLGWPHGGQSP
CSLKWPTPVPRKATPEVPTICCNQICNHRLFLSRVQLAIINGMNGAPQMSTASSMYGEQTLLSCCHVGISV
QLCQVF

The following DNA sequence Seq-2575 <SEQ ID NO. 116> was identified in *H. sapiens*:

TTATTTTTTATTGATGATAGTTGAGAAATTTCTTCCAGCTTCACAACTTGTTATTGGAAATGTCAAGTGAA
TTTCTGGACTGTTGTCTGAATTCGTTTGTTAGGGCTCCCATTACAAAATACCACAGACTGGGTGACTTATA
CAACATGAATTTATTTTCACAAATTCTGGAGTCTGGATGTTCATGATCAAGGTGTCGGCAGGTTTGGTTTC
TTCTGAGGCCTCTCTCCTTGGCTCACAGAAGGACGTCTTCTTGCTGTGTCTTCACATGGCTGTCCCTCTGT
GTGTGTTTGTGTCCTAATCTCCTCTTCTTATAAGGACACCTGTTATGCTCCATCAGGGCCCATCTTAATGA
CTCCATTTTAACTTAATTAGCTCTTTAAAGATATTTTCTCCAAATACAGACACATTTTAAAGTACTGAGGA
GGCGTTTTAACTTTATGAATTTTAGGGGGGACACAAATCAGCTTATAACATAACAATGTTATGTTTAACAT
AACAAGTTTAACAAAACTTGCAAAAACATCTTTCAGATACTTTCATATTAAAATTTTCCTTGTGCAGTGAT
TGATCCTAAGTACTCTGAACTATTGACATTTTAACTAATTTGATGGCTAGGTCCTCATTATATTAGTTTAT
TGCCATCTCTTTGTAGACATCAAAGCAGCAAAAAAGGAA

The following amino acid sequence <SEQ ID NO. 244> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 116:

IFYLRNFFQLHNLLLEMSSEFLDCCLNSFVRAPITKYHRLGDLYNMNLFSQILESGCSSRCRQVWFLLRPL
SLAHRRTSSCCVFTWLSLCVCLCPNLLFLGHLLCSIRAHLNDSILTLALRYFLQIQTHFKVLRRRFNFMNF
RGDTNQLITQCYVHNKFNKTCKNIFQILSYNFPCAVIDPKYSELLTFLIWLGPHYISLLPSLCRHQSSKKG

The following DNA sequence Seq-2576 <SEQ ID NO. 117> was identified in *H. sapiens*:

GCCTTCCCCCCAGTCCCTGTCACAATGGATGGTGCTCAAAAACACGTGTATTGAATGCATTCTTTGAGTCA
GTGGTTGAATGCCTCTCACACCAGAGGGTGAGGTCTTGGAAGGGAGGAACTGCAGTTGGTAGGCTCTGGGT
CAAGGAGACCTGGATTCAAGTCCTGCCTCTCTAACTTACTGGCTTTGGGCAAATTACTTAACCTGGCTGAG
CCTTGGTTTCCTCATCTGTGAAATGCAGTTGCTGTGAGGATTTGATGAGCCAATGCACATGAGACTTGAGG
AGTACTGGCTGTGAATGCAAGGGTTGCCCTTGGTGCTCTCTCTTCATCCCTGGAGCCTGGCCCTGTGCAGG
GCTGGGAGGATGCAGGTGCTTGGAAGATGGGCTTGGCTAATGGGAGTCGCTGTGGCTTTTGCAGATGAATA
TGAATGCCAGGCCTGCCCGAATAACGAGTGGTCCTACCAGAGTGAGACCTCCTGCTTCAAGCGGCAGCTGG
TCTTCCTGGAATGGCATGAGGCACCCACCATCGCTGTGGCCCTGCTGGCCGCCCTGGGCTTCCTCAGCACC
CTGGCCATCCTGGTGATATTCTGGAGGCACTTCCAGACACCCATAGTTCGCTCGGCTGGGGGCCCCATGTG
CTTCCTGATGCTGACACTGCTGCTGGTGGCATACATGGTGGTCCCGGTGTACGTGGGG

The following amino acid sequence <SEQ ID NO. 245> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 117:

PSPQSLSQWMVLKNTCIECILVSGMPLTPEGEVLEGRNCSWALGQGDLDSSPASLTYWLWANYLTWLSLGF
LICEMQLLGFDEPMHMRLEEYWLMQGLPLVLSLHPWSLALCRAGRMQVLGRWAWLMGVAVAFADEYECQAC
PNNEWSYQSETSCFKRQLVFLEWHEAPTIAVALLAALGFLSTLAILVIFWRHFQTPIVRSAGGPMCFLMLT
LLLVAYMVVPVYVG

The following DNA sequence Seq-2577 <SEQ ID NO. 118> was identified in *H. sapiens*:

ATGTGTATATATATATAAAAAAGGTAATATAAAATATATGTAATATAAATATATGTAAAATATTAAATATA
CATAAAATGTATGTAAAATATAAAAATATATAAAATATATGTAAAATATAAAATATATGTAATATTTATAC
TATAAAAATATATATAAATGCAGGGGTTTAAAATCATATTTATATGATATATATGTAAAATCATATATGTG
TGTGTGTGTATATATACATATATGATTTTAAAACCCTGCATTTTTTATATTATTGGAGTAGAACCAATCCT
TTTGTTGATAACTAAAAGCTAGCCACGGATACATTTGCCTAGATTTTTTGATTTATTTGTGAGCTGCCAAG
GATGGCAACAACTTCAAGACTTTCTTTGGCAATAAAACATAGTCAACATATTTAAATAAACAAACATTTAA
ATAAATATACCGTAAAGTATAATTAAACATTCTTTAAAATGAAAACACTTGATTAAAATTATTCCTAAATG
GAGTATCAAGATTTTGATACTTATAAGAGATTATGGTGTCTGTGAAAGAATTGATAAATAGATCAATAGAA

GTCAAGAAAGTGGTTACTTTTGGAGAAGGGATACAGTGGGGATTTTGATTGCTACCAATGTCCAATTTCTT
GACCCTGTGTGATAGTAAATCATTTGACTCTACA

The following amino acid sequence <SEQ ID NO. 246> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 118:

VESNDVLLSHRVKKLDIGSNQNPHCIPSPKVTTFLTSIDLFINSFTDTIISYKYQNLDTPFRNNFNQVFSF
RMFNYTLRYIYLNVCLFKYVDYVLLPKKVLKLLPSLAAHKIKKSRQMYPWLAFSYQQKDWFYSNNIKNAGF
NHICIYTHTHIYDFTYISYKYDFKPLHLYIFLYKYYIYFIFYIYFIYFYILHTFYVYLIFYIYLYYIYFIL
PFLYIYTH

The following DNA sequence Seq-2578 SEQ ID NO. 119> was identified in *H. sapiens*:

CACACACCTTCTTCGTTGTCTGAACCCTGCAAAAAACATTCATAAAACTATTAGATTTAGATAACATATTT
CAAATAGGTTTATTCTTTAATTCAATTCATATTTACTGAATACTATTTGCCAAAAACAGTGGTAAATACTG
AAGATATAAAGATGAGTAAGTTCTTGTACTCAAGAAGCTTATGGTCTAGTAAAAAAAAAAATGCAGTCATG
CAAACAAATAAAGACAAAAGGATATCAAATGTGAAACAATACATACAGAGCTTTACACAGAAATATGTAGT
CATTACAAGGAGAGTTGGAAAATGCTTTAAAACAAGGTAATAGCTGATCTGAGTTTTGAAAGCTGAGCACG
TCTTTAGCAAGAAAGCAAGCATAATAGATGACTCAAAAGCCAAAATGTTACTATCCGAGTGACATGGATTG
CTGTTATAAGATAGGTAGAATCTAAAAATTGTGTTTATGTGTGTCTAAAATATGTCTCTGCGTTGCACT

The following amino acid sequence <SEQ ID NO. 247> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 119:

VQRRDIFTHINTIFRFYLSYNSNPCHSDSNILAFESSIMLAFLLKTCSAFKTQISYYLVLKHFPTLLVMTT
YFCVKLCMYCFTFDILLSLFVCMTAFFFLLDHKLLEYKNLLIFISSVFTTVFGKYSVNMNIKETYLKYVII
FYECFLQGSDNEEGV

The following DNA sequence Seq-2579 <SEQ ID NO. 120> was identified in *H. sapiens*:

CTCCTGGAGCCTGGACTCACATACATCACCATGACTGAGCCATAGAAGAAAGAAACAACCAAGAAATGGGA
AGCACATGTAGAGAAAGCTTTGTTCCTGCCTGAGCCAGCTGGGACCCACAGAACAGCTCGCAAAACTAAGA
TATGGGACCCAAGAATGTAGAGGAAGGTGATGAAGATGATGAGAGAGCTTACTGTAGCACAAGTCAGAGTA
GTTTTGGGAACTGGGGCACAGGACAGTGCCAGCAATGGTCCCAGGTTACAGAAAAAATGGTCAGTGATGTT
AGGGCCACAGAAAGGCACTCGGGACATAAGCACTGCAGGCATCAGTATGGATAGAAAACCACCTGCCCTGC
AGAAGGCCACTAATCGGACACACAGGTGGTGAGTCATGACTGTGGGATAATGCAAAGGTCGACAGATGGTA
AGGAACCGATCAAAGGACATCACAGACAGAAAGTAGCCTTCTGCAGCACACATGGAGAAGTAGAAGAACTG
GAGCAGGCAGCCAGCATAGGAGATGCTCTTGATATGGGAGATGAGATTGGCCAACATTTTGGGACATCAGA
ACTAATGCAGCAGATCTCCAGGAAAGAGAAATTAGCCAAGAGGATGTACATAGGTGTGTGGAGTTTCTGGC
TTGACCACACAGCGCAGATGATGGATGTGTTACCCA

The following amino acid sequence <SEQ ID NO. 248> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 120:
GHIHHLRCVVKPETPHTYVHPLGFLFPGDLLHFCPKMLANLISHIKSISYAGCLLQFFYFSMCAAEGYFLS
VMSFDRFLTICRPLHYPTVMTHHLCVRLVAFCRAGGFLSILMPAVLMSRVPFCGPNITDHFFCNLGPLLAL
SCAPVPKTTLTCATVSSLIIFITFLYILGSHILVLRAVLWVPAGSGRNKAFSTCASHFLVVSFFYGSVMVM
YVSPGSR

The following DNA sequence Seq-2580 <SEQ ID NO. 121> was identified in *H. sapiens*:

GTGTGACCTTGGGCGTGTCACATGACTTCCTGAACTGTGCTGTTGTCTGTAAAGGGAGGTGGTCAGACTGG
GATCCTCTCCAGGATTGCAGGCCTGTCTTATTATCTTGTTTTACTTCAGTCTGCCAGGATTTCTTTCTGGA
ACTCCCTGTGGTCCCAGTTGCCGGATTTCAGAGATTGCTGTGGGGAATGCCATGGAATAGAATCTGGCCAC
CTTGAGCTGAGAAAGGTGTTTGTGATTGATGGTTGATGCCACCAAGCAAACAGGGTTAAGCAACTTGACTG
CCTGCCTGCTGCTTTTAAAAAGGCAGCTGACGACCTAATTCTGTTTAGAATTAGGGGCGAAGCTAAGGAAA
CTGGCTCAGGCTGTGAGTATCATCTCTAGATTCAGATTTCTGGGACCACATCAGAAACCAGGTTTTATGTG
GACCTTTGATGGGCAGTGTGGTGTGCAACGTGGGGGACTGTGGGTTTTAGACTGGGCAGTTCTGGCTGGGG
ATTCCAGTTCTACCCCTTAGCAGCATTGTTGGGAGGACGAAAGGGAAATGCCGGATGGGAAGTGCAAGATG
CAGC

The following amino acid sequence <SEQ ID NO. 249> is the predicted

amino acid sequence derived from the DNA sequence of SEQ ID NO. 121:

AASCTSHPAFPFRPPNNAAKGNWNPQPELPSLKPTVPHVAHHTAHQRSTNLVSDVVPEIIRYSQPEPVSLA
SPLILNRIRSSAAFLKAAGRQSSCLTLFAWWHQPSITNTFLSSRWPDSIPWHSPQQSLKSGNWDHREFQKE
ILADSKTRDRPAILERIPVPPPFTDNSTVQEVMHAQGH

The following DNA sequence Seq-2581 <SEQ ID NO. 122> was identified in *H. sapiens*:

TCTAAAATATTCAAACCATGACATTTGTGAATTTTCTATGAAAAAAAGAGGGAAGTTAGCTCGTTATTCAG
ATGATAAAAGCCTCTTCCTTCTCTATTTTTCCATTTGCACCATCACACCAGGGGAAATTATGGAGATGAGA
AATACTACCCCAGACTTTATTCTCCTGGGACTCTTTAACCACACCAGAGCCCACCAAGTCCTCTTCATGAT
GGTTCTGAGTATCGTTTTGACCTCCCTGTTTGGCAATTCCCTCATGATTCTCCTGATTCACCGGGACCGGC
CGGCTCCACACGCCCATGTACTTCCTCCTGAGCCAACTCTCCCTCATGGACGTGATGCTGGTTTCCACCAC
TGTGCCCAAAATGGCGGCTGACTACTTGACCGGAAATAAGGCCATCTCCCGCGCTGGCTGTGGTGTGCAGA
TCTTCTTCCTGCTCACCCTGGGTGGTGGAGAGTGCTTCCTCTTAGCAGCCATGGCCTATGACCGCTATGCG
GCTGTCTGCCACCCACTCCGATATCCCACTCTCATGAGCTGGCAGCTGTGCCTGAGGATGACCATGTCGTC
CTGGCTCCTGGGTGCAGCTGACGGGCTCCTGC

The following amino acid sequence <SEQ ID NO. 250> is a predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 122:

LKYSNHDICEFSMKKRGKLARYSDDKSLFLLYFSICTITPGEIMEMRNTTPDFILLGLFNHTRAHQVLFM
MVLSIVLTSLFGNSLMILLIHRD

The following amino acid sequence <SEQ ID NO. 251> is a predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 122:

RLHTPMYFLLSQLSLMDVMLVSTTVPKMAADYLTGNKAISRAGCGVQIFFLLTLGGGECFLLAAMAYDRYA
AVCHPLRYPTLMSWQLCLRMTMSSWLLGAADGLL

The following DNA sequence Seq-2582 <SEQ ID NO. 123> was identified in *H. sapiens*:

TTCCCAGCTCTACCACTAGCCTGCTGGGCGTGTTCTGCAAACCTCTCTCCCTCCCTGGGCCTCAGTTTTTG
TATTTGCAAAATGGCAGTGGGTCAGACCCCTTAGCCTCAAAGGGCCCTCCCAACCTCTGGCACTTGAGCAT
CTCTGAGCCTGCTGGGCCACCTGTCCCAGTGCCTCTTGGGCTTTGGAAGTTGAATGCTGCAACCCCAAGCC
CCAGTTTCAGGTAGGGATGAGCCCATTGCCCAATGCTGGGGTCCGAGTGGGCCTGAAGGCTCCCAGAGGAC
CACGTTCTCAGCCCTGGATGGGCAGGGACCCTGGAGACCTGGCCTGTGTGGACACAGGGGAGTAAGTACTG
GGACTGAGCCTGTAGTTTTGCTTCTTCCACCCAACCCGTTGGGGGTCGTTCTCACAGCTTGGTGCTGGGTA
CACCAGGGGACTCACCATTGGAGGGATCCGATGGGTTCCAAGGTGCACAAAACAGACCCCCAGGTCATCCT
CAGGTGGTCTACACAGCCTGTGGCTAAAGCAACTGCTGTCTCCAGCACTTCTTAGCTTCAGTCTGGTGAAA
GGAAGAAAGTCCCCTTGGCAGTGTCTTACAGGCAGTCATAGAGGGACCCCACAGCCTGGCCAAAATGCTCA
ATTTCAGAAAATCCCAGACTCAT

The following amino acid sequence <SEQ ID NO. 252> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 123:

MSLGFSEIEHFGQAVGSLYDCLDTAKGTFFLSPDSEVLETAVALATGCVDHLRMTWGSVLCTLEPIGSLQW
VPWCTQHQAVRTTPNGLGGRSKTTGSVPVLTPLCPHRPGLQGPCPSRAENVVLWEPSGPLGPQHWAMGSSL
PETGAWGCSIQLPKPKRHWDRWPSRLRDAQVPEVGRALGGVPTAILQIQKLRPREGERFAEHAQQASGRAG

The following DNA sequence Seq-2583 <SEQ ID NO. 124> was identified in *H. sapiens*:

TAGGTGGTGAGCTGAATCAATCTTCATTACTAAGGTGTCAGGTGCTCAGGCTAAACCTGCAGCTTTCCAAT
AGGGAAAACATTCAGTCTAGTAGCTTGTTCTGCTACTAGACTGCCTCAGTGAATGAGTAACTGACTGGATT
AAACAAAACACCCCAGAAATATTTACCAAGAAGGTAAGGTCCAAAAGGAAGGTAGTGAAAGGAAATGTACT
CTGATCATGAAATGGTTGGTTGATGAGCAAGTCAAGCTTGAAGATTTATCTCTTTTCTTCATTCAGAAAAG
CAACTGAAATGCAAACTGGTGCTATTAATAACATAGTCCTTGAAGACAACCTAAAAATAGTTCCTAAAATG
CCATTTGTAACTGTAATTTTGCATCTCAATCATTGGCAGTTTGGAATGACAGTATTTTGTACAGCAAGATG
ATGCACATTATAATACTATATATAGAGAGAGAGACATGCATGTGCTCCTCCTTCTTCCCCACACAAATCAC
CCGGAGGTCATAAAAATGTTTAAGTTCCACCAGGAGTAAGCAAAAATTTAACAAGGAAATACATACTCATT
TTACATTTAGGTAATTAAGTAGTAATCTCCTTGATGTTAATTTTTATTTCTCCAAGTTAAAGTTCTTGCTT

ATATGAACTCTTGCTTTCTAA

The following amino acid sequence <SEQ ID NO. 253> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 124:

RWAESIFITKVSGAQAKPAAFQGKHSVLVLLLDCLSEVTDWIKQNTPEIFTKKVRSKRKVVKGNVLSNGWL
MSKSSLKIYLFSSFRKATEMQTGAINNIVLEDNLKIVPKMPFVTVILHLNHWQFGMTVFCTARCTLYYIRE
RHACAPPSSPHKSPGGHKNVVPPGVSKNLTRKYILILHLGNVVISLMLIFISPSSSCLYELLLS

The following DNA sequence Seq-2584 <SEQ ID NO. 125> was identified in *H. sapiens*:

TACCAAGTAAAAATTTTAAAGCCGATTATTTTATTTCTGCTTTCATGAATTTCCAGTGTAATGGAGAAGAT
AAGAGGAAATAAGTAAGCATGTATCTGGCCAATTACTTATATGTTTTATAGAGTTACAGACATAATTATAA
ATCAGGTAGGTTAGGGAGATACAAGTTTCATTTAAGAAATGAACTGTAGGGGAAGGTAGTGGGGAAGAGGG
ATCAGGAGAGGTTGGCCAATGGGTACAAAGTTACAGTTAGGAAGAATAAGTTCTGGTGTTTTGTTGTACAG
TAGGGTGCCTCTGGCAAACAACAATGTAGTGTATACTTTTAAGATAGCTAGAAGAGAAGATTTTGAATGTT
ATCACCACTAAGAAATGATCAATGTTTAAAGTAGTAAATACAGTAATGACCATGATTTGATCATCATGCAA
TGTATACACTCATTGAAACATCACACTGTACCCCATAAATGTGTACAATCATTATGTCAATTATAAATATT
AAAAATTAATTTTAAGAAGAAACGCAGAAAAAAAATGTTAACAGTGTTCTAAAGGAAGGGACAGTTGCATCG
GAAAGACTTGGAAATGTGTAAGGTGACAGTCAAGAGAAATGGGAGTTTATGGTGACCGAGTAGGATATGGA
TCAAGGTAACCACCAGCAATGGGTGTGAAGCATTGCATATG

The following amino acid sequence <SEQ ID NO. 254> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 125:

YAMLHTHCWWLPSISYSVTINSHFSLSPYTFPSLSDATVPSFRTLLTFFSAFLLKINFYLLTLYTFMGYSV
MFQVYTLHDDQIMVITVFTTLNIDHFLVVITFKIFSSSYLKSIHYIVVCQRHPTVQQNTRTYSSLLCTHWP
TSPDPSSPLPSPTVHFLNETCISLTYLIYNYVCNSIKHISNWPDTCLLISSYLLHYTGNSKQKNNRLNFYL
V

The following DNA sequence Seq-2585 <SEQ ID NO. 126> was identified in *H. sapiens*:

GGCTGCGTGCATCATTTCCCTTGTCACGCTGGACAGGGAAACGCGGTTGTGCTCTGGCTCCTGGGCTTCCG
CATGCGCAGGGAACGCCGTCTCCATCTACATCCTCAACCTGGCTGCGGCAGACTTCCTCTTCCTCAGCGGC
CACGTTATACGTTCCGCCTCACTCCTCATCAATATCTGTCATCCCATCTCCAAAATCCTCATTCCTGTGAT
GACCTTTCTATACTTTACAGGCCTGAGCTTTCTGAGTGCCATGAGCACCGAGCGCTGCCTGTGCGTCCTGT
GGCCCATCTGGTACCGCTGCCTCCTCCCCCCACACACCTGTCAGCGGTCGTGTGTGTCTTGCTTTGGGCCC
TGTCCCTACTGCGGAGCATCCTGGAGTGAATGTTCTGTGACTTCCTGTTTAGTGATGCTGATTCTATTTGG
TGTCAACCATCAGATTTCATCACAGTCGTGTGGCTGATTTTTTTATGTGTGGTTCTCTGTGGGTCCAGCCT
GGTCCTGCTGATTAGGATTCTCTGTGGATCCTGGAAGATGCCTCTGACCGGGCTGTACGTGACGATCCTGC
TCACAGTGCTAGTCTTCCTACTCCGCAGCCTGCCCTTCGGCATTCGGTGGGCTCTGTCTACTGGGATACAC
CTG

The following amino acid sequence <SEQ ID NO. 255> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 126:

AACIISLVTLDRETRLCSGSWASACAGNAVSIYILNLAAADFLFLSGHVIRSASLLINICHPISKILIPVM
TFLYFTGLSFLSAMSTERCLCVLWPIWYRCLLPPHTCQRSCVSCFGPCPYCGASWSECSVTSCLVMLILFG
VNHQISSQSCGFFYVWFSVGPAWSCLGFSVDPGRCLPGCTRSCSQCSSYSAACPSAFGGLCLLGYT

The following DNA sequence Seq-2586 <SEQ ID NO. 127> was identified in *H. sapiens*:

AACAAAACAACTCCTGTTATTCCGAAGGAGAAAAGAAACATTTTCTGTTTTAATTTGTGATCATCAGGGTC
TTCTAAAGCATAGGGCTCAGGGAAGGAGGGTTATCAACATCTGGCCAAGGGCTGGAGATGGAAATGTTTCC
AGACCCTAAAGCAAGAAAAAGATCAGCAGGTTAGAGAAAAAGTAAGATGGCCACTTACTTAGAGTGAATTT
AGATAAGAATAAAAGCCGTGCCCCAGGAGTAGGCAAGAGGCTGATTATTGAGATCCTGTAACCCATGGGAA
GGAACCCTAATCTTATGATGCTGGTGATGAGAAAGTGTTGGTGGGGTAGAGTAAGAGAACACATTAATCTG
CTTTGCCTCATGGAAAGAATAAATTCTGGTAGACATATGTAGATGCAGAGAGTGAGCTATTATAGTTTTTG
TAAGAGAGATTATGGTTTGACTTATGGTGACAGTGATGGACATGGTGAGCAATGGATGCCTTTGTGATCTG
CAGACTTTTTACCTGACACACTGAGTGCATGATCATGCCATTTACTGAGAGGTGACAATGG

The following amino acid sequence <SEQ ID NO. 256> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 127:

PLSPLSKWHDHALSVSGKKSADHKGIHCSPCPSLSPVKPSLLQKLLTLCIYICLPEFILSMRQSRLMCSLT
LPHQHFLITSIIRLGFLPMGYRISIISLLPTPGARLLFLSKFTLSKWPSYFFSNLLIFFLLGLETFPSPAL
GQMLITLLPALCFRRPSQIKTENVSFLLRNNRSCFV

The following DNA sequence Seq-2587 <SEQ ID NO. 128> was identified in *H. sapiens*:

CTTTGGGCTCTGATAAATTTTTTTTCTGATTTTTTGCAGGGAACACATTTGAAATAATAGGACTGAAAAT
TATGAGGAAGAAACATTTGTCCTTGGTGTTTCTGAAATATGTGAACCAAACCCCAATGCCTGCACTTTTGC
TCTCACAAACTTCTGACATGAGGCACAGATTTTTACAAAACAGCTTAACATAGAAGTCTCACAAAATGTGC
AGATTTCCTCAGATCCCAAAAACAATGGAAAAGCACTCAGACCACAAGAGCTTCATGGGAATAGCAGAAAG
AAGAGGCGAACTTTGGCTGTCACTGTGAATGCCCTGGAATGTTAGTGGATGAACAGAGAAGCCTTAGAAGA
TTTAAGAGCATAATAAGCATAGGGTAGGAAATTTCCACCTGTGGCAGCAAAAGAAGTAAATTTAGAATTTT
CCAGAACCAATTTCTTTGAAGCAGAACTTCCAACACCACATTTTTAAGGTTTTTCTCCTTGGCCTTTGCAC
CTCTCATCTTTGTTATTTGTTCATTCTTCCCTATTGGGCTGTTGCCTATTATTGTCTCTCTTTTTACATTC
CAAAGAACATTTCCTTTACTGTAGGACA

The following amino acid sequence <SEQ ID NO. 257> is the predicted amino acid sequence derived from the DNA sequence of SEQ ID NO. 128:

LWALINFFSDFFAGNTFEIIGLKIMRKKHLSLVFLKYVNQTPMPALLLSQTSDMRHRFLQNSLTKSHKMCR
FPQIPKTMEKHSDHKSFMGIAERRGELWLSLMPWNVSGTEKPKIEHNKHRVGNFHLWQQKKINFPEPISLK
QNFQHHIFKVFLLGLCTSHLCYLFILPYWAVAYYCLSFYIPKNISFTVG

EXAMPLE 2: CLONING OF nGPCR-x

[000239] cDNAs may be sequenced directly using an AB1377 or ABI373A fluorescence-based sequencer (Perkin Elmer/Applied Biosystems Division, PE/ABD, Foster City, CA) and the ABI PRISM Ready Dye-Deoxy Terminator kit with Taq FS polymerase. Each ABI cycle sequencing reaction contains about 0.5μg of plasmid DNA. Cycle-sequencing is performed using an initial denaturation at 98°C for 1 min, followed by 50 cycles: 98°C for 30 sec, annealing at 50°C for 30 sec, and extension at 60°C for 4 min. Temperature cycles and times are controlled by a Perkin-Elmer 9600 thermocycler. Extension products are purified using Centriflex gel filtration (Advanced Genetic Technologies Corp., Gaithersburg, MD). Each reaction product is loaded by pipette onto the column, which is then centrifuged in a swinging bucket centrifuge (Sorvall model RT6000B table top centrifuge) at 1500 x g for 4 min at room temperature. Column-purified samples are dried under vacuum for about 40 min and then dissolved in 5μl of a DNA loading solution (83% deionized formamide, 8.3 mM EDTA, and 1.6 mg/ml Blue Dextran). The samples are then heated to 90°C for three min and loaded into the gel sample wells for sequence analysis by the ABI377 sequencer. Sequence analysis is performed by importing ABI373A files into the Sequencher program (Gene Codes, Ann Arbor, MI). Generally, sequence reads of 700 bp are obtained. Potential sequencing errors are minimized by obtaining sequence information from both DNA strands and by re-sequencing difficult areas using primers at different locations until all sequencing ambiguities are removed.

[000240] To isolate a cDNA clone encoding full length nGPCR, a DNA fragment corresponding to a nucleotide sequence selected from the group consisting of SEQ ID NO:1 to SEQ ID NO:128, or a portion thereof, can be used as a probe for hybridization screening of a phage cDNA library. The DNA fragment is amplified by the polymerase chain reaction (PCR) method. The PCR reaction mixture of 50µl contains polymerase mixture (0.2mM dNTPs, 1x PCR Buffer and 0.75µl Expand High Fidelity Polymerase (Roche Biochemicals)), 1µg of 3206491 plasmid, and 50pmoles of forward primer and 50pmoles of reverse primer. The primers are preferably 10 to 25 nucleotides in length and are determined by procedures well known to those skilled in the art. Amplification is performed in an Applied Biosystems PE2400 thermocycler, using the following program: 95°C for 15 seconds, 52°C for 30 seconds and 72°C for 90 seconds; repeated for 25 cycles. The amplified product is separated from the plasmid by agarose gel electrophoresis, and purified by Qiaquick gel extraction kit (Qiagen).

[000241] A lambda phage library containing cDNAs cloned into lambda ZAPII phage-vector is plated with E. coli XL-1 blue host, on 15 cm LB-agar plates at a density of 50,000 pfu per plate, and grown overnight at 37°C; (plated as described by Sambrook *et al.*, *supra*). Phage plaques are transferred to nylon membranes (Amersham Hybond NJ), denatured for 2 minutes in denaturation solution (0.5 M NaOH, 1.5 M NaCl), renatured for 5 minutes in renaturation solution (1 M Tris pH 7.5, 1.5 M NaCl), and washed briefly in 2xSSC (20x SSC: 3 M NaCl, 0.3 M Na-citrate). Filter membranes are dried and incubated at 80°C for 120 minutes to cross-link the phage DNA to the membranes.

[000242] The membranes are hybridized with a DNA probe prepared as described above. A DNA fragment (25ng) is labeled with α-^{32}P-dCTP (NEN) using Rediprime random priming (Amersham Pharmacia Biotech), according to the manufacturer's instructions. Labeled DNA is separated from unincorporated nucleotides by S200 spin columns (Amersham Pharmacia Biotech), denatured at 95°C for 5 minutes and kept on ice. The DNA-containing membranes (above) are pre-hybridized in 50ml ExpressHyb (Clontech) solution at 68°C for 90 minutes. Subsequently, the labeled DNA probe is added to the hybridization solution, and the probe is left to hybridize to the membranes at 68°C for 70 minutes. The membranes are washed five times in 2x SSC, 0.1% SDS at 42°C for 5 minutes each, and finally washed 30 minutes in 0.1x SSC, 0.2% SDS. Filters are exposed to Kodak XAR film (Eastman Kodak Company, Rochester, N.Y., USA) with an intensifying screen at –80°C for 16 hours. One positive colony is isolated from the plates, and re-plated with about 1000 pfu on a 15 cm LB plate. Plating, plaque lift to filters and hybridization are performed as described above. About four positive phage plaques are isolated form this secondary screening.

[000243] cDNA containing plasmids (pBluescript SK-) are rescued from the isolated phages by in vivo excision by culturing XL-1 blue cells co-infected with the isolated phages and with the Excision helper phage, as described by the manufacturer (Stratagene). XL-blue cells containing the plasmids are plated on LB plates and grown at 37°C for 16 hours. Colonies (18) from each plate are replated on LB plates and grown. One colony from each plate is stricken onto a nylon filter in an ordered array, and the filter is placed on a LB plate to raise the colonies. The filter is then hybridized with a labeled probe as described above. About three positive colonies are selected and grown up in LB medium. Plasmid DNA is isolated from the three clones by Qiagen Midi Kit (Qiagen) according to the manufacturer's instructions. The size of the insert is determined by digesting the plasmid with the restriction enzymes NotI and SalI, which establishes an insert size. The sequence of the entire insert is determined by automated sequencing on both strands of the plasmids.

EXAMPLE 3: SUBCLONING OF THE CODING REGION OF nGPCR-X VIA PCR

[000244] Additional experiments may be conducted to subclone the coding region of nGPCR and place the isolated coding region into a useful vector. Two additional PCR primers are designed based on the coding region of nGPCR, corresponding to either end. To protect against exonucleolytic attack during subsequent exposure to enzymes, *e.g.*, Taq polymerase, primers are routinely synthesized with a protective run of nucleotides at the 5' end that were not necessarily complementary to the desired target.

[000245] PCR is performed in a 50µl reaction containing 34µl H_2O, 5 µl 10X TT buffer (140 mM ammonium sulfate, 0.1% gelatin, 0.6 M Tris-tricine, pH 8.4), 5µl 15mM $MgSO_4$, 2µl dNTP mixture (dGTP, dATP, dTTP, and dCTP, each at 10 mM), 3µl genomic phage DNA (0.25µg/µl), 0.3µl Primer 1 (1µg/µl), 0.3µl Primer 2 (1µg/µl), 0.4µl High Fidelity Taq polymerase (Boehringer Mannheim). The PCR reaction was started with 1 cycle of 94°C for 2 minutes; followed by 25 cycles at 94°C for 30 seconds, 55°C for 30 seconds, and 72°C for 1.3 minutes.

[000246] The contents from the PCR reaction are loaded onto a 2% agarose gel and fractionated. The DNA band of expected size is excised from the gel, placed in a GenElute Agarose spin column (Supelco) and spun for 10 minutes at maximum speed in a microfuge. The eluted DNA is precipitated with ethanol and resuspended in 6µl H_2O for ligation.

[000247] The PCR-amplified DNA fragment containing the coding region is cloned into pCR2.1 using a protocol standard in the art. In particular, the ligation reaction consists of 6µl of GPCR DNA, 1µl 10X ligation buffer, 2µl pCR2.1 (25ng/µl, Invitrogen), and 1µl T4 DNA ligase (Invitrogen). The reaction mixture is incubated overnight at 14°C and the reaction is then stopped by heating at 65°C for 10 minutes. Two microliters of the ligation reaction are

transformed into One Shot cells (Invitrogen) and plated onto ampicillin plates. A single colony containing a recombinant pCR2.1 bearing an insert is used to inoculate a 5ml culture of LB medium. Plasmid DNA is purified using the Concert Rapid Plasmid Miniprep System (GibcoBRL) and sequenced. Following confirmation of the sequence, a 50 ml culture of LB medium is inoculated with the transformed One Shot cells, cultured, and processed using a Qiagen Plasmid Midi Kit to yield purified pCR-GPCR.

EXAMPLE 4: HYBRIDIZATION ANALYSIS TO DEMONSTRATE nGPCR-X EXPRESSION IN BRAIN

[000248] The expression of nGPCR-x in mammals, such as the rat, may be investigated by *in situ* hybridization histochemistry. To investigate expression in the brain, for example, coronal and sagittal rat brain cryosections (20μm thick) are prepared using a Reichert-Jung cryostat. Individual sections are thaw-mounted onto silanized, nuclease-free slides (CEL Associates, Inc., Houston, TX), and stored at -80°C. Sections are processed starting with post-fixation in cold 4% paraformaldehyde, rinsed in cold phosphate-buffered saline (PBS), acetylated using acetic anhydride in triethanolamine buffer, and dehydrated through a series of alcohol washes in 70%, 95%, and 100% alcohol at room temperature. Subsequently, sections are delipidated in chloroform, followed by rehydration through successive exposure to 100% and 95% alcohol at room temperature. Microscope slides containing processed cryosections are allowed to air dry prior to hybridization. Other tissues may be assayed in a similar fashion.

[000249] A nGPCR-x-specific probe is generated using PCR. Following PCR amplification, the fragment is digested with restriction enzymes and cloned into pBluescript II cleaved with the same enzymes. For production of a probe specific for the sense strand of nGPCR-x, the nGPCR-x clone in pBluescript II is linearized with a suitable restriction enzyme, which provides a substrate for labeled run-off transcripts (*i.e.*, cRNA riboprobes) using the vector-borne T7 promoter and commercially available T7 RNA polymerase. A probe specific for the antisense strand of nGPCR-x is also readily prepared using the nGPCR-x clone in pBluescript II by cleaving the recombinant plasmid with a suitable restriction enzyme to generate a linearized substrate for the production of labeled run-off cRNA transcripts using the T3 promoter and cognate polymerase. The riboprobes are labeled with [^{35}S]-UTP to yield a specific activity of about 0.40 x 10^6 cpm/pmol for antisense riboprobes and about 0.65 x 10^6 cpm/pmol for sense-strand riboprobes. Each riboprobe is subsequently denatured and added (2 pmol/ml) to hybridization buffer which contained 50% formamide, 10% dextran, 0.3 M NaCl, 10 mM Tris (pH 8.0), 1 mM EDTA, 1X Denhardt's Solution, and 10 mM dithiothreitol. Microscope slides containing sequential brain cryosections are independently exposed to 45μl of hybridization

solution per slide and silanized cover slips are placed over the sections being exposed to hybridization solution. Sections are incubated overnight (15-18 hours) at 52°C to allow hybridization to occur. Equivalent series of cryosections are exposed to sense or antisense nGPCR-x-specific cRNA riboprobes.

[000250] Following the hybridization period, coverslips are washed off the slides in 1X SSC, followed by RNase A treatment involving the exposure of slides to 20 μg/ml RNase A in a buffer containing 10mM Tris-HCl (pH 7.4), 0.5M EDTA, and 0.5M NaCl for 45 minutes at 37°C. The cryosections are then subjected to three high-stringency washes in 0.1 X SSC at 52°C for 20 minutes each. Following the series of washes, cryosections are dehydrated by consecutive exposure to 70%, 95%, and 100% ammonium acetate in alcohol, followed by air drying and exposure to Kodak BioMax™ MR-1 film. After 13 days of exposure, the film is developed. Based on these results, slides containing tissue that hybridized, as shown by film autoradiograms, are coated with Kodak NTB-2 nuclear track emulsion and the slides are stored in the dark for 32 days. The slides are then developed and counterstained with hematoxylin. Emulsion-coated sections are analyzed microscopically to determine the specificity of labeling. The signal is determined to be specific if autoradiographic grains (generated by antisense probe hybridization) are clearly associated with cresyl violate-stained cell bodies. Autoradiographic grains found between cell bodies indicates non-specific binding of the probe.

[000251] As discussed above, it is well known that GPCRs are expressed in many different tissues and regions, including in the brain. Expression of nGPCR-x in the brain provides an indication that modulators of nGPCR-x activity have utility for treating neurological disorders, including but not limited to, mental disorder, affective disorders, ADHD/ADD (*i.e.*, Attention Deficit Hyperactivity Disorder/Attention Deficit Disorder), and neural disorders such as Alzheimer's disease, Parkinson's disease, migraine, and senile dementia. Some other diseases for which modulators of nGPCR-x may have utility include depression, anxiety, bipolar disease, epilepsy, neuritis, neurasthenia, neuropathy, neuroses, and the like. Use of nGPCR-x modulators, including nGPCR-x ligands and anti-nGPCR-x antibodies, to treat individuals having such disease states is intended as an aspect of the invention.

EXAMPLE 5: TISSUE EXPRESSION PROFILING

[000252] A PCR-based system (RapidScan™ Gene Expression Panel, OriGene Technologies, Rockville, MD) may be used to generate a comprehensive expression profile of the putative nGPCR-x in human tissue, and in human brain regions. The RapidScan Expression Panel is comprised of first-strand cDNAs from various human tissues and brain regions that are serially diluted over a 4-log range and arrayed into a multi-well PCR plate. Human tissues in the array

may include: brain, heart, kidney, spleen, liver, colon, lung, small intestine, muscle, stomach, testis, placenta, salivary gland, thyroid, adrenal gland, pancreas, ovary, uterus, prostate, skin, PBL, bone marrow, fetal brain, and fetal liver.

[000253] Expression of nGPCR-x in various tissues is detected using PCR primers designed based on the available sequence of the receptor that will prime the synthesis of a predetermined size fragment in the presence of the appropriate cDNA.

[000254] PCR is performed in a 50μl reaction containing 34μl H_2O, 5μl 10X TT buffer (140 mM ammonium sulfate, 0.1% gelatin, 0.6 M Tris-tricine, pH 8.4), 5μl 15mM $MgSO_4$, 2μl dNTP mixture (dGTP, dATP, dTTP, and dCTP, each at 10mM), 0.3μl forward primer (1μg/μl), 0.3μl reverse primer (1μg/μl), 0.4μl High Fidelity Taq polymerase (Boehringer Mannheim). The PCR reaction mixture is added to each well of the PCR plate. The plate is placed in a MJ Research PTC100 thermocycler, and is then exposed to the following cycling parameters: Pre-soak 94°C for 3 min; denaturation at 94°C for 30 seconds; annealing at primer 57°C for 45 seconds; extension 72°C for 2 minutes; for 35 cycles. PCR productions are then separated and analyzed by electrophoresis on a 1.2% agarose gel stained with ethidium bromide.

[000255] The 4-log dilution range of cDNA deposited on the plate ensures that the amplification reaction is within the linear range and, hence, facilitates semi-quantitative determination of relative mRNA accumulation in the various tissues or brain regions examined.

EXAMPLE 6: NORTHERN BLOT ANALYSIS

[000256] Northern blots are performed to examine the expression of nGPCR-x mRNA. The sense orientation oligonucleotide and the antisense-orientation oligonucleotide, described above, are used as primers to amplify a portion of the GPCR-x cDNA sequence selected from the group consisting of SEQ ID NO:1 to SEQ ID NO:128.

[000257] Multiple human tissue northern blots from Clontech (Human II # 7767-1) are hybridized with the probe. Pre-hybridization is carried out at 42 C for 4 hours in 5xSSC, 1X Denhardt's reagent, 0.1% SDS, 50% formamide, 250 mg/ml salmon sperm DNA. Hybridization is performed overnight at 42°C in the same mixture with the addition of about $1.5x10^6$ cpm/ml of labeled probe.

[000258] The probe is labeled with α-^{32}P-dCTP by Rediprime™ DNA labeling system (Amersham Pharmacia), purified on Nick Column™ (Amersham Pharmacia) and added to the hybridization solution. The filters are washed several times at 42°C in 0.2x SSC, 0.1% SDS. Filters are exposed to Kodak XAR film (Eastman Kodak Company, Rochester, N.Y., USA) with intensifying screen at –80°C.

EXAMPLE 7: RECOMBINANT EXPRESSION OF nGPCR-X IN EUKARYOTIC HOST CELLS

A. Expression of nGPCR-x in Mammalian Cells

[000259] To produce nGPCR-x protein, a nGPCR-x-encoding polynucleotide is expressed in a suitable host cell using a suitable expression vector and standard genetic engineering techniques. For example, the nGPCR-x-encoding sequence described in Example 1 is subcloned into the commercial expression vector pzeoSV2 (Invitrogen, San Diego, CA) and transfected into Chinese Hamster Ovary (CHO) cells using the transfection reagent FuGENE6™ (Boehringer-Mannheim) and the transfection protocol provided in the product insert. Other eukaryotic cell lines, including human embryonic kidney (HEK-293) and COS cells, are suitable as well. Cells stably expressing nGPCR-x are selected by growth in the presence of 100μg/ml zeocin (Stratagene, LaJolla, CA). Optionally, nGPCR-x may be purified from the cells using standard chromatographic techniques. To facilitate purification, antisera is raised against one or more synthetic peptide sequences that correspond to portions of the nGPCR-x amino acid sequence, and the antisera is used to affinity purify nGPCR-x. The nGPCR-x also may be expressed in-frame with a tag sequence (*e.g.*, polyhistidine, hemagluttinin, FLAG) to facilitate purification. Moreover, it will be appreciated that many of the uses for nGPCR-x polypeptides, such as assays described below, do not require purification of nGPCR-x from the host cell.

B. Expression of nGPCR-x in HEK-293 cells

[000260] For expression of nGPCR-x in mammalian cells HEK293 (transformed human, primary embryonic kidney cells), a plasmid bearing the relevant nGPCR-x coding sequence is prepared, using vector pSecTag2A (Invitrogen). Vector pSecTag2A contains the murine IgK chain leader sequence for secretion, the c-myc epitope for detection of the recombinant protein with the anti-myc antibody, a C-terminal polyhistidine for purification with nickel chelate chromatography, and a Zeocin resistant gene for selection of stable transfectants. The forward primer for amplification of this GPCR cDNA is determined by routine procedures and preferably contains a 5' extension of nucleotides to introduce the *HindIII* cloning site and nucleotides matching the GPCR sequence. The reverse primer is also determined by routine procedures and preferably contains a 5' extension of nucleotides to introduce an *XhoI* restriction site for cloning and nucleotides corresponding to the reverse complement of the nGPCR-x sequence. The PCR conditions are 55°C as the annealing temperature. The PCR product is gel purified and cloned into the *HindIII-XhoI* sites of the vector.

[000261] The DNA is purified using Qiagen chromatography columns and transfected into HEK-293 cells using DOTAP™ transfection media (Boehringer Mannheim, Indianapolis, IN). Transiently transfected cells are tested for expression after 24 hours of transfection, using

western blots probed with anti-His and anti-nGPCR-x peptide antibodies. Permanently transfected cells are selected with Zeocin and propagated. Production of the recombinant protein is detected from both cells and media by western blots probed with anti-His, anti-Myc or anti-GPCR peptide antibodies.

C. Expression of nGPCR-x in COS cells

[000262] For expression of the nGPCR-x in COS7 cells, a polynucleotide molecule having a sequence selected from the group consisting of SEQ ID NO:1 to SEQ ID NO:128 can be cloned into vector p3-CI. This vector is a pUC18-derived plasmid that contains the HCMV (human cytomegalovirus) promoter-intron located upstream from the bGH (bovine growth hormone) polyadenylation sequence and a multiple cloning site. In addition, the plasmid contains the dhrf (dihydrofolate reductase) gene which provides selection in the presence of the drug methotrexane (MTX) for selection of stable transformants.

[000263] The forward primer is determined by routine procedures and preferably contains a 5' extension which introduces an *XbaI* restriction site for cloning, followed by nucleotides which correspond to a sequence selected from the group consisting of SEQ ID NO:1 to SEQ ID NO:128. The reverse primer is also determined by routine procedures and preferably contains 5'- extension of nucleotides which introduces a *SalI* cloning site followed by nucleotides which correspond to the reverse complement of a sequence selected from the group consisting of SEQ ID NO:1 to SEQ ID NO:128. The PCR consists of an initial denaturation step of 5 min at 95°C 30 cycles of 30 sec denaturation at 95°C, 30 sec annealing at 58°C and 30 sec extension at 72°C, followed by 5 min extension at 72°C. The PCR product is gel purified and ligated into the *XbaI* and *SalI* sites of vector p3-CI. This construct is transformed into *E. coli* cells for amplification and DNA purification. The DNA is purified with Qiagen chromatography columns and transfected into COS 7 cells using Lipofectamine™ reagent from BRL, following the manufacturer's protocols. Forty-eight and 72 hours after transfection, the media and the cells are tested for recombinant protein expression.

[000264] nGPCR-x expressed from a COS cell culture can be purified by concentrating the cell-growth media to about 10 mg of protein/ml, and purifying the protein by, for example, chromatography. Purified nGPCR-x is concentrated to 0.5 mg/ml in an Amicon concentrator fitted with a YM-10 membrane and stored at -80°C.

D. Expression of nGPCR-x in Insect Cells

[000265] For expression of nGPCR-x in a baculovirus system, a polynucleotide molecule having a sequence selected from the group consisting of SEQ ID NO:1 to SEQ ID NO:128 can be amplified by PCR. The forward primer is determined by routine procedures and preferably contains a 5' extension which adds the *NdeI* cloning site, followed by nucleotides which

correspond to a sequence selected from the group consisting of SEQ ID NO:1 to SEQ ID NO:128. The reverse primer is also determined by routine procedures and preferably contains a 5' extension which introduces the *KpnI* cloning site, followed by nucleotides which correspond to the reverse complement of a sequence selected from the group consisting of SEQ ID NO:1 to SEQ ID NO:128.

[000266] The PCR product is gel purified, digested with *NdeI* and *KpnI*, and cloned into the corresponding sites of vector pACHTL-A (Pharmingen, San Diego, CA). The pAcHTL expression vector contains the strong polyhedrin promoter of the *Autographa californica* nuclear polyhedrosis virus (AcMNPV), and a 6XHis tag upstream from the multiple cloning site. A protein kinase site for phosphorylation and a thrombin site for excision of the recombinant protein precede the multiple cloning site is also present. Of course, many other baculovirus vectors could be used in place of pAcHTL-A, such as pAc373, pVL941 and pAcIM1. Other suitable vectors for the expression of GPCR polypeptides can be used, provided that the vector construct includes appropriately located signals for transcription, translation, and trafficking, such as an in-frame AUG and a signal peptide, as required. Such vectors are described in Luckow *et al.*, Virology 170:31-39, among others.

[000267] The virus is grown and isolated using standard baculovirus expression methods, such as those described in Summers *et al.* (A Manual of Methods for Baculovirus Vectors and Insect Cell Culture Procedures, Texas Agricultural Experimental Station Bulletin No. 1555 (1987)).

[000268] In a preferred embodiment, pAcHLT-A containing nGPCR-x gene is introduced into baculovirus using the "BaculoGold™ transfection kit (Pharmingen, San Diego, CA) using methods established by the manufacturer. Individual virus isolates are analyzed for protein production by radiolabeling infected cells with ^{35}S-methionine at 24 hours post infection. Infected cells are harvested at 48 hours post infection, and the labeled proteins are visualized by SDS-PAGE. Viruses exhibiting high expression levels can be isolated and used for scaled up expression.

[000269] For expression of a nGPCR-x polypeptide in a Sf9 cells, a polynucleotide molecule having a sequence selected from the group consisting of SEQ ID NO:1 to SEQ ID NO:128 can be amplified by PCR using the primers and methods described above for baculovirus expression. The nGPCR-x cDNA is cloned into vector pAcHLT-A (Pharmingen) for expression in Sf9 insect. The insert is cloned into the *NdeI* and *KpnI* sites, after elimination of an internal *NdeI* site (using the same primers described above for expression in baculovirus). DNA is purified with Qiagen chromatography columns and expressed in Sf9 cells. Preliminary Western blot experiments from non-purified plaques are tested for the presence of the recombinant

protein of the expected size which reacted with the GPCR-specific antibody. These results are confirmed after further purification and expression optimization in HiG5 cells.

EXAMPLE 8: INTERACTION TRAP/TWO-HYBRID SYSTEM

[000270] In order to assay for nGPCR-x-interacting proteins, the interaction trap/two-hybrid library screening method can be used. This assay was first described in Fields *et al*, *Nature,* **1989**, *340*, 245, which is incorporated herein by reference in its entirety. A protocol is published in Current Protocols in Molecular Biology 1999, John Wiley & Sons, NY, and Ausubel, F. M. *et al.* 1992, Short protocols in molecular biology, Fourth edition, Greene and Wiley-interscience, NY, each of which is incorporated herein by reference in its entirety. Kits are available from Clontech, Palo Alto, CA (Matchmaker Two-Hybrid System 3).

[000271] A fusion of the nucleotide sequences encoding all or partial nGPCR-x and the yeast transcription factor GAL4 DNA-binding domain (DNA-BD) is constructed in an appropriate plasmid (*i.e.*, pGBKT7) using standard subcloning techniques. Similarly, a GAL4 active domain (AD) fusion library is constructed in a second plasmid (*i.e.*, pGADT7) from cDNA of potential GPCR-binding proteins (for protocols on forming cDNA libraries, see Sambrook *et al.* 1989, Molecular cloning: a laboratory manual, second edition, Cold Spring Harbor Press, Cold Spring Harbor, NY), which is incorporated herein by reference in its entirety. The DNA-BD/nGPCR-x fusion construct is verified by sequencing, and tested for autonomous reporter gene activation and cell toxicity, both of which would prevent a successful two-hybrid analysis. Similar controls are performed with the AD/library fusion construct to ensure expression in host cells and lack of transcriptional activity. Yeast cells are transformed (*ca.* 105 transformants/mg DNA) with both the nGPCR-x and library fusion plasmids according to standard procedures (Ausubel *et al.*, 1992, Short protocols in molecular biology, fourth edition, Greene and Wiley-interscience, NY, which is incorporated herein by reference in its entirety). *In vivo* binding of DNA-BD/nGPCR-x with AD/library proteins results in transcription of specific yeast plasmid reporter genes (*i.e.*, lacZ, HIS3, ADE2, LEU2). Yeast cells are plated on nutrient-deficient media to screen for expression of reporter genes. Colonies are dually assayed for β-galactosidase activity upon growth in Xgal (5-bromo-4-chloro-3-indolyl-β-D-galactoside) supplemented media (filter assay for β-galactosidase activity is described in Breeden *et al.*, Cold Spring Harb. Symp. Quant. Biol., 1985, 50, 643, which is incorporated herein by reference in its entirety). Positive AD-library plasmids are rescued from transformants and reintroduced into the original yeast strain as well as other strains containing unrelated DNA-BD fusion proteins to confirm specific nGPCR-x/library protein interactions. Insert DNA is sequenced to verify the

presence of an open reading frame fused to GAL4 AD and to determine the identity of the nGPCR-x-binding protein.

EXAMPLE 9: MOBILITY SHIFT DNA-BINDING ASSAY USING GEL ELECTROPHORESIS

[000272] A gel electrophoresis mobility shift assay can rapidly detect specific protein-DNA interactions. Protocols are widely available in such manuals as Sambrook *et al.* **1989**, *Molecular cloning: a laboratory* manual, second edition, Cold Spring Harbor Press, Cold Spring Harbor, NY and Ausubel, F. M. *et al.*, 1992, Short Protocols in Molecular Biology, fourth edition, Greene and Wiley-interscience, NY, each of which is incorporated herein by reference in its entirety.

[000273] Probe DNA (<300 bp) is obtained from synthetic oligonucleotides, restriction endonuclease fragments, or PCR fragments and end-labeled with ^{32}P. An aliquot of purified nGPCR-x (*ca.* 15 μg) or crude nGPCR-x extract (*ca.* 15 ng) is incubated at constant temperature (in the range 22-37 C) for at least 30 minutes in 10-15 μl of buffer (*i.e.* TAE or TBE, pH 8.0-8.5) containing radiolabeled probe DNA, nonspecific carrier DNA (*ca.* 1 μg), BSA (300 μg/ml), and 10% (v/v) glycerol. The reaction mixture is then loaded onto a polyacrylamide gel and run at 30-35 mA until good separation of free probe DNA from protein-DNA complexes occurs. The gel is then dried and bands corresponding to free DNA and protein-DNA complexes are detected by autoradiography.

EXAMPLE 10: ANTIBODIES TO nGPCR-X

[000274] Standard techniques are employed to generate polyclonal or monoclonal antibodies to the nGPCR-x receptor, and to generate useful antigen-binding fragments thereof or variants thereof, including "humanized" variants. Such protocols can be found, for example, in Sambrook *et al.* (1989) and Harlow *et al.* (Eds.), Antibodies A Laboratory Manual; Cold Spring Harbor Laboratory; Cold Spring Harbor, NY (1988). In one embodiment, recombinant nGPCR-x polypeptides (or cells or cell membranes containing such polypeptides) are used as antigen to generate the antibodies. In another embodiment, one or more peptides having amino acid sequences corresponding to an immunogenic portion of nGPCR-x (*e.g.*, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, or more amino acids) are used as antigen. Peptides corresponding to extracellular portions of nGPCR-x, especially hydrophilic extracellular portions, are preferred. The antigen may be mixed with an adjuvant or linked to a hapten to increase antibody production.

A. Polyclonal or Monoclonal antibodies

[000275] As one exemplary protocol, recombinant nGPCR-x or a synthetic fragment thereof is used to immunize a mouse for generation of monoclonal antibodies (or larger mammal, such as a rabbit, for polyclonal antibodies). To increase antigenicity, peptides are conjugated to Keyhole Lympet Hemocyanin (Pierce), according to the manufacturer's recommendations. For an initial injection, the antigen is emulsified with Freund's Complete Adjuvant and injected subcutaneously. At intervals of two to three weeks, additional aliquots of nGPCR-x antigen are emulsified with Freund's Incomplete Adjuvant and injected subcutaneously. Prior to the final booster injection, a serum sample is taken from the immunized mice and assayed bywestern blot to confirm the presence of antibodies that immunoreact with nGPCR-x. Serum from the immunized animals may be used as polyclonal antisera or used to isolate polyclonal antibodies that recognize nGPCR-x. Alternatively, the mice are sacrificed and their spleen removed for generation of monoclonal antibodies.

[000276] To generate monoclonal antibodies, the spleens are placed in 10 ml serum-free RPMI 1640, and single cell suspensions are formed by grinding the spleens in serum-free RPMI 1640, supplemented with 2 mM L-glutamine, 1 mM sodium pyruvate, 100 units/ml penicillin, and 100 μg/ml streptomycin (RPMI) (Gibco, Canada). The cell suspensions are filtered and washed by centrifugation and resuspended in serum-free RPMI. Thymocytes taken from three naive Balb/c mice are prepared in a similar manner and used as a Feeder Layer. NS-1 myeloma cells, kept in log phase in RPMI with 10% fetal bovine serum (FBS) (Hyclone Laboratories, Inc., Logan, Utah) for three days prior to fusion, are centrifuged and washed as well.

[000277] To produce hybridoma fusions, spleen cells from the immunized mice are combined with NS-1 cells and centrifuged, and the supernatant is aspirated. The cell pellet is dislodged by tapping the tube, and 2 ml of 37°C PEG 1500 (50% in 75 mM HEPES, pH 8.0) (Boehringer-Mannheim) is stirred into the pellet, followed by the addition of serum-free RPMI. Thereafter, the cells are centrifuged, resuspended in RPMI containing 15% FBS, 100 μM sodium hypoxanthine, 0.4 μM aminopterin, 16 μM thymidine (HAT) (Gibco), 25 units/ml IL-6 (Boehringer-Mannheim) and 1.5 x 10^6 thymocytes/ml, and plated into 10 Corning flat-bottom 96-well tissue culture plates (Corning, Corning New York).

[000278] On days 2, 4, and 6 after the fusion, 100μl of medium is removed from the wells of the fusion plates and replaced with fresh medium. On day 8, the fusions are screened by ELISA, testing for the presence of mouse IgG that binds to nGPCR-x. Selected fusion wells are further cloned by dilution until monoclonal cultures producing anti-nGPCR-x antibodies are obtained.

B. Humanization of anti-nGPCR-x monoclonal antibodies

[000279] The expression pattern of nGPCR-x as reported herein and the proven track record of GPCRs as targets for therapeutic intervention suggest therapeutic indications for nGPCR-x

inhibitors (antagonists). nGPCR-x-neutralizing antibodies comprise one class of therapeutics useful as nGPCR-x antagonists. Following are protocols to improve the utility of anti-nGPCR-x monoclonal antibodies as therapeutics in humans by "humanizing" the monoclonal antibodies to improve their serum half-life and render them less immunogenic in human hosts (*i.e.*, to prevent human antibody response to non-human anti-nGPCR-x antibodies).

[000280] The principles of humanization have been described in the literature and are facilitated by the modular arrangement of antibody proteins. To minimize the possibility of binding complement, a humanized antibody of the IgG4 isotype is preferred.

[000281] For example, a level of humanization is achieved by generating chimeric antibodies comprising the variable domains of non-human antibody proteins of interest with the constant domains of human antibody molecules. (See, *e.g.*, Morrison *et al.*, Adv. Immunol., 44:65-92 (1989)). The variable domains of nGPCR-x-neutralizing anti-nGPCR-x antibodies are cloned from the genomic DNA of a B-cell hybridoma or from cDNA generated from mRNA isolated from the hybridoma of interest. The V region gene fragments are linked to exons encoding human antibody constant domains, and the resultant construct is expressed in suitable mammalian host cells (*e.g.*, myeloma or CHO cells).

[000282] To achieve an even greater level of humanization, only those portions of the variable region gene fragments that encode antigen-binding complementarity determining regions ("CDR") of the non-human monoclonal antibody genes are cloned into human antibody sequences. (See, *e.g.*, Jones *et al.*, Nature 321:522-525 (1986); Riechmann *et al.*, Nature 332:323-327 (1988); Verhoeyen *et al.*, Science 239:1534-36 (1988); and Tempest *et al.*, Bio/Technology 9: 266-71 (1991)). If necessary, the β-sheet framework of the human antibody surrounding the CDR3 regions also is modified to more closely mirror the three dimensional structure of the antigen-binding domain of the original monoclonal antibody. (See Kettleborough *et al.*, Protein Engin., 4:773-783 (1991); and Foote *et al.*, J. Mol. Biol., 224:487-499 (1992)).

[000283] In an alternative approach, the surface of a non-human monoclonal antibody of interest is humanized by altering selected surface residues of the non-human antibody, *e.g.*, by site-directed mutagenesis, while retaining all of the interior and contacting residues of the non-human antibody. See Padlan, Molecular Immunol., 28(4/5):489-98 (1991).

[000284] The foregoing approaches are employed using nGPCR-x-neutralizing anti-nGPCR-x monoclonal antibodies and the hybridomas that produce them to generate humanized nGPCR-x-neutralizing antibodies useful as therapeutics to treat or palliate conditions wherein nGPCR-x expression or ligand-mediated nGPCR-x signaling is detrimental.

C. Human nGPCR-x-Neutralizing Antibodies from Phage Display

[000285] Human nGPCR-x-neutralizing antibodies are generated by phage display techniques such as those described in Aujame *et al.*, Human Antibodies 8(4):155-168 (1997); Hoogenboom, TIBTECH 15:62-70 (1997); and Rader *et al.*, Curr. Opin. Biotechnol. 8:503-508 (1997), all of which are incorporated by reference. For example, antibody variable regions in the form of Fab fragments or linked single chain Fv fragments are fused to the amino terminus of filamentous phage minor coat protein pIII. Expression of the fusion protein and incorporation thereof into the mature phage coat results in phage particles that present an antibody on their surface and contain the genetic material encoding the antibody. A phage library comprising such constructs is expressed in bacteria, and the library is screened for nGPCR-x-specific phage-antibodies using labeled or immobilized nGPCR-x as antigen-probe.

D. Human nGPCR-x-neutralizing antibodies from transgenic mice

[000286] Human nGPCR-x-neutralizing antibodies are generated in transgenic mice essentially as described in Bruggemann *et al.*, Immunol. Today 17(8):391-97 (1996) and Bruggemann *et al.*, Curr. Opin. Biotechnol. 8:455-58 (1997). Transgenic mice carrying human V-gene segments in germline configuration and that express these transgenes in their lymphoid tissue are immunized with a nGPCR-x composition using conventional immunization protocols. Hybridomas are generated using B cells from the immunized mice using conventional protocols and screened to identify hybridomas secreting anti-nGPCR-x human antibodies (*e.g.*, as described above).

EXAMPLE 11: ASSAYS TO IDENTIFY MODULATORS OF nGPCR-X ACTIVITY

[000287] Set forth below are several nonlimiting assays for identifying modulators (agonists and antagonists) of nGPCR-x activity. Among the modulators that can be identified by these assays are natural ligand compounds of the receptor; synthetic analogs and derivatives of natural ligands; antibodies, antibody fragments, and/or antibody-like compounds derived from natural antibodies or from antibody-like combinatorial libraries; and/or synthetic compounds identified by high-throughput screening of libraries; and the like. All modulators that bind nGPCR-x are useful for identifying nGPCR-x in tissue samples (*e.g.*, for diagnostic purposes, pathological purposes, and the like). Agonist and antagonist modulators are useful for up-regulating and down-regulating nGPCR-x activity, respectively, to treat disease states characterized by abnormal levels of nGPCR-x activity. The assays may be performed using single putative modulators, and/or may be performed using a known agonist in combination with candidate antagonists (or visa versa).

A. cAMP Assays

[000288] In one type of assay, levels of cyclic adenosine monophosphate (cAMP) are measured in nGPCR-x-transfected cells that have been exposed to candidate modulator compounds.

Protocols for cAMP assays have been described in the literature. (See, *e.g.*, Sutherland *et al.*, Circulation 37: 279 (1968); Frandsen *et al.*, Life Sciences 18: 529-541 (1976); Dooley *et al.*, Journal of Pharmacology and Experimental Therapeutics 283 (2): 735-41 (1997); and George *et al.*, Journal of Biomolecular Screening 2 (4): 235-40 (1997)). An exemplary protocol for such an assay, using an Adenylyl Cyclase Activation FlashPlate® Assay from NEN™ Life Science Products, is set forth below.

[000289] Briefly, the nGPCR-x coding sequence (*e.g.*, a cDNA or intronless genomic DNA) is subcloned into a commercial expression vector, such as pzeoSV2 (Invitrogen), and transiently transfected into Chinese Hamster Ovary (CHO) cells using known methods, such as the transfection protocol provided by Boehringer-Mannheim when supplying the FuGENE 6 transfection reagent. Transfected CHO cells are seeded into 96-well microplates from the FlashPlate® assay kit, which are coated with solid scintillant to which antisera to cAMP has been bound. For a control, some wells are seeded with wild type (untransfected) CHO cells. Other wells in the plate receive various amounts of a cAMP standard solution for use in creating a standard curve.

[000290] One or more test compounds (*i.e.*, candidate modulators) are added to the cells in each well, with water and/or compound-free medium/diluent serving as a control or controls. After treatment, cAMP is allowed to accumulate in the cells for exactly 15 minutes at room temperature. The assay is terminated by the addition of lysis buffer containing [^{125}I]-labeled cAMP, and the plate is counted using a Packard Topcount™ 96-well microplate scintillation counter. Unlabeled cAMP from the lysed cells (or from standards) and fixed amounts of [^{125}I]-cAMP compete for antibody bound to the plate. A standard curve is constructed, and cAMP values for the unknowns are obtained by interpolation. Changes in intracellular cAMP levels of cells in response to exposure to a test compound are indicative of nGPCR-x modulating activity. Modulators that act as agonists of receptors which couple to the G_s subtype of G proteins will stimulate production of cAMP, leading to a measurable 3-10 fold increase in cAMP levels. Agonists of receptors which couple to the $G_{i/o}$ subtype of G proteins will inhibit forskolin-stimulated cAMP production, leading to a measurable decrease in cAMP levels of 50-100%. Modulators that act as inverse agonists will reverse these effects at receptors that are either constitutively active or activated by known agonists.

B. Aequorin Assays

[000291] In another assay, cells (*e.g.*, CHO cells) are transiently co-transfected with both a nGPCR-x expression construct and a construct that encodes the photoprotein apoaquorin. In the presence of the cofactor coelenterazine, apoaquorin will emit a measurable luminescence that is proportional to the amount of intracellular (cytoplasmic) free calcium. (See generally, Cobbold,

et al. "Aequorin measurements of cytoplasmic free calcium," *In*: McCormack J.G. and Cobbold P.H., eds., *Cellular Calcium: A Practical Approach*. Oxford:IRL Press (1991); Stables *et al*, Analytical Biochemistry 252: 115-26 (1997); and Haugland, Handbook of Fluorescent Probes and Research Chemicals. Sixth edition. Eugene OR: Molecular Probes (1996).)

[000292] In one exemplary assay, nGPCR-x is subcloned into the commercial expression vector pzeoSV2 (Invitrogen) and transiently co-transfected along with a construct that encodes the photoprotein apoaquorin (Molecular Probes, Eugene, OR) into CHO cells using the transfection reagent FuGENE 6 (Boehringer-Mannheim) and the transfection protocol provided in the product insert.

[000293] The cells are cultured for 24 hours at 37℃ in MEM (Gibco/BRL, Gaithersburg, MD) supplemented with 10% fetal bovine serum, 2 mM glutamine, 10 U/ml penicillin and 10 μg/ml streptomycin, at which time the medium is changed to serum-free MEM containing 5 μM coelenterazine (Molecular Probes, Eugene, OR). Culturing is then continued for two additional hours at 37°C. Subsequently, cells are detached from the plate using VERSEN (Gibco/BRL), washed, and resuspended at 200,000 cells/ml in serum-free MEM.

[000294] Dilutions of candidate nGPCR-x modulator compounds are prepared in serum-free MEM and dispensed into wells of an opaque 96-well assay plate at 50 μl/well. Plates are then loaded onto an MLX microtiter plate luminometer (Dynex Technologies, Inc., Chantilly, VA). The instrument is programmed to dispense 50μl cell suspensions into each well, one well at a time, and immediately read luminescence for 15 seconds. Dose-response curves for the candidate modulators are constructed using the area under the curve for each light signal peak. Data are analyzed with SlideWrite, using the equation for a one-site ligand, and EC_{50} values are obtained. Changes in luminescence caused by the compounds are considered indicative of modulatory activity. Modulators that act as agonists at receptors which couple to the G_q subtype of G proteins give an increase in luminescence of up to 100 fold. Modulators that act as inverse agonists will reverse this effect at receptors that are either constitutively active or activated by known agonists.

C. Luciferase Reporter Gene Assay

[000295] The photoprotein luciferase provides another useful tool for assaying for modulators of nGPCR-x activity. Cells (*e.g.*, CHO cells or COS 7 cells) are transiently co-transfected with both a nGPCR-x expression construct (*e.g.*, nGPCR-x in pzeoSV2) and a reporter construct which includes a gene for the luciferase protein downstream from a transcription factor binding site, such as the cAMP-response element (CRE), AP-1, or NF-kappa B. Agonist binding to receptors coupled to the G_s subtype of G proteins leads to increases in cAMP, thereby activating the CRE transcription factor and resulting in expression of the luciferase gene. Agonist binding

to receptors coupled to the G_q subtype of G protein leads to production of diacylglycerol that activates protein kinase C, which activates the AP-1 or NF-kappa B transcription factors, in turn resulting in expression of the luciferase gene. Expression levels of luciferase reflect the activation status of the signaling events. (See generally, George *et al*, Journal of Biomolecular Screening 2(4): 235-240 (1997); and Stratowa *et al.*, Current Opinion in Biotechnology 6: 574-581 (1995)). Luciferase activity may be quantitatively measured using, *e.g*, luciferase assay reagents that are commercially available from Promega (Madison, WI).

[000296] In one exemplary assay, CHO cells are plated in 24-well culture dishes at a density of 100,000 cells/well one day prior to transfection and cultured at 37℃ in MEM (Gibco/BRL) supplemented with 10% fetal bovine serum, 2 mM glutamine, 10 U/ml penicillin and 10 μg/ml streptomycin. Cells are transiently co-transfected with both a nGPCR-x expression construct and a reporter construct containing the luciferase gene. The reporter plasmids CRE-luciferase, AP-1-luciferase and NF-kappaB-luciferase may be purchased from Stratagene (LaJolla, CA). Transfections are performed using the FuGENE 6 transfection reagent (Boehringer-Mannheim) according to the supplier's instructions. Cells transfected with the reporter construct alone are used as a control. Twenty-four hours after transfection, cells are washed once with PBS pre-warmed to 37°C. Serum-free MEM is then added to the cells either alone (control) or with one or more candidate modulators and the cells are incubated at 37℃ for five hours. Thereafter, cells are washed once with ice-cold PBS and lysed by the addition of 100 μl of lysis buffer per well from the luciferase assay kit supplied by Promega. After incubation for 15 minutes at room temperature, 15μl of the lysate is mixed with 50 μl of substrate solution (Promega) in an opaque-white, 96-well plate, and the luminescence is read immediately on a Wallace model 1450 MicroBeta scintillation and luminescence counter (Wallace Instruments, Gaithersburg, MD).

[000297] Differences in luminescence in the presence versus the absence of a candidate modulator compound are indicative of modulatory activity. Receptors that are either constitutively active or activated by agonists typically give a 3 to 20-fold stimulation of luminescence compared to cells transfected with the reporter gene alone. Modulators that act as inverse agonists will reverse this effect.

D. Intracellular calcium measurement using FLIPR

[000298] Changes in intracellular calcium levels are another recognized indicator of G protein-coupled receptor activity, and such assays can be employed to screen for modulators of nGPCR-x activity. For example, CHO cells stably transfected with a nGPCR-x expression vector are plated at a density of 4 x 10^4 cells/well in Packard black-walled, 96-well plates specially designed to discriminate fluorescence signals emanating from the various wells on theplate.

The cells are incubated for 60 minutes at 37°C in modified Dulbecco's PBS (D-PBS) containing 36 mg/L pyruvate and 1 g/L glucose with the addition of 1% fetal bovine serum and one of four calcium indicator dyes (Fluo-3™ AM, Fluo-4™ AM, Calcium Green™-1 AM, or Oregon Green™ 488 BAPTA-1 AM), each at a concentration of 4 μM. Plates are washed once with modified D-PBS without 1% fetal bovine serum and incubated for 10 minutes at 37°C to remove residual dye from the cellular membrane. In addition, a series of washes with modified D-PBS without 1% fetal bovine serum is performed immediately prior to activation of the calcium response.

[000299] A calcium response is initiated by the addition of one or more candidate receptor agonist compounds, calcium ionophore A23187 (10 μM; positive control), or ATP (4 μM; positive control). Fluorescence is measured by Molecular Device's FLIPR with an argon laser (excitation at 488 nm). (See, *e.g.*, Kuntzweiler *et al.*, Drug Development Research, 44(1):14-20 (1998)). The F-stop for the detector camera was set at 2.5 and the length of exposure was 0.4 milliseconds. Basal fluorescence of cells was measured for 20 seconds prior to addition of candidate agonist, ATP, or A23187, and the basal fluorescence level was subtracted from the response signal. The calcium signal is measured for approximately 200 seconds, taking readings every two seconds. Calcium ionophore A23187 and ATP increase the calcium signal 200% above baseline levels. In general, activated GPCRs increase the calcium signal approximately 10-15% above baseline signal.

E. Mitogenesis Assay

[000300] In a mitogenesis assay, the ability of candidate modulators to induce or inhibit nGPCR-x-mediated cell division is determined. (*See, e.g.*, Lajiness *et al*, Journal of Pharmacology and Experimental Therapeutics 267(3): 1573-1581 (1993)). For example, CHO cells stably expressing nGPCR-x are seeded into 96-well plates at a density of 5000 cells/well and grown at 37°C in MEM with 10% fetal calf serum for 48 hours, at which time the cells are rinsed twice with serum-free MEM. After rinsing, 80μl of fresh MEM, or MEM containing a known mitogen, is added along with 20μl MEM containing varying concentrations of one or more candidate modulators or test compounds diluted in serum-free medium. As controls, some wells on each plate receive serum-free medium alone, and some receive medium containing 10% fetal bovine serum. Untransfected cells or cells transfected with vector alone also may serve as controls.

[000301] After culture for 16-18 hours, 1μ Ci of [^{3}H]-thymidine (2 Ci/mmol) is added to the wells and cells are incubated for an additional 2 hours at 37°C. The cells are trypsinized and collected on filter mats with a cell harvester (Tomtec); the filters are then counted in a Betaplate counter. The incorporation of [^{3}H]-thymidine in serum-free test wells is compared to the results achieved

in cells stimulated with serum (positive control). Use of multiple concentrations of test compounds permits creation and analysis of dose-response curves using the non-linear, least squares fit equation: A = B x [C/ (D + C)] + G where A is the percent of serum stimulation; B is the maximal effect minus baseline; C is the EC_{50}; D is the concentration of the compound; and G is the maximal effect. Parameters B, C and G are determined by Simplex optimization.

[000302] Agonists that bind to the receptor are expected to increase [^{3}H]-thymidine incorporation into cells, showing up to 80% of the response to serum. Antagonists that bind to the receptor will inhibit the stimulation seen with a known agonist by up to 100%.

F. [^{35}S]GTPγS Binding Assay

[000303] Because G protein-coupled receptors signal through intracellular G proteins whose activity involves GTP binding and hydrolysis to yield bound GDP, measurement of binding of the non-hydrolyzable GTP analog [^{35}S]GTPγS in the presence and absence of candidate modulators provides another assay for modulator activity. (*See, e.g.*, Kowal *et al*, Neuropharmacology 37:179-187 (1998).)

[000304] In one exemplary assay, cells stably transfected with a nGPCR-x expression vector are grown in 10 cm tissue culture dishes to subconfluence, rinsed once with 5 ml of ice-cold Ca^{2+}/Mg^{2+}-free phosphate-buffered saline, and scraped into 5 ml of the same buffer. Cells are pelleted by centrifugation (500 x *g*, 5 minutes), resuspended in TEE buffer (25 mM Tris, pH 7.5, 5 mM EDTA, 5 mM EGTA), and frozen in liquid nitrogen. After thawing, the cells are homogenized using a Dounce homogenizer (one ml TEE per plate of cells), and centrifuged at 1,000 x *g* for 5 minutes to remove nuclei and unbroken cells.

[000305] The homogenate supernatant is centrifuged at 20,000 x *g* for 20 minutes to isolate the membrane fraction, and the membrane pellet is washed once with TEE and resuspended in binding buffer (20 mM HEPES, pH 7.5, 150 mM NaCl, 10 mM $MgCl_2$, 1 mM EDTA). The resuspended membranes can be frozen in liquid nitrogen and stored at -70°C until use.

[000306] Aliquots of cell membranes prepared as described above and stored at -70°C are thawed, homogenized, and diluted into buffer containing 20 mM HEPES, 10 mM $MgCl_2$, 1 mM EDTA, 120 mM NaCl, 10μM GDP, and 0.2 mM ascorbate, at a concentration of 10-50 μg/ml. In a final volume of 90μl, homogenates are incubated with varying concentrations of candidate modulator compounds or 100 μM GTP for 30 minutes at 30°C and then placed on ice. To each sample, 10 μl guanosine 5'-O-(3[^{35}S]thio) triphosphate (NEN, 1200 Ci/mmol; [^{35}S]-GTPγS), was added to a final concentration of 100-200 pM. Samples are incubated at 30°C for an additional 30 minutes, 1 ml of 10mM HEPES, pH 7.4, 10 mM $MgCl_2$, at 4°C is added and the reaction is stopped by filtration.

[000307] Samples are filtered over Whatman GF/B filters and the filters are washed with 20 ml ice-cold 10 mM HEPES, pH 7.4, 10 mM $MgCl_2$. Filters are counted by liquid scintillation spectroscopy. Nonspecific binding of [^{35}S]-GTPγS is measured in the presence of 100 μM GTP and subtracted from the total. Compounds are selected that modulate the amount of [^{35}S]-GTPγS binding in the cells, compared to untransfected control cells. Activation of receptors by agonists gives up to a five-fold increase in [^{35}S]GTPγS binding. This response is blocked by antagonists.

G. MAP Kinase Activity Assay

[000308] Evaluation of MAP kinase activity in cells expressing a GPCR provides another assay to identify modulators of GPCR activity. (See, *e.g.*, Lajiness *et al.*, Journal of Pharmacology and Experimental Therapeutics 267(3):1573-1581 (1993) and Boulton *et al.*, Cell 65:663-675 (1991).)

[000309] In one embodiment, CHO cells stably transfected with nGPCR-x are seeded into 6-well plates at a density of 70,000 cells/well 48 hours prior to the assay. During this 48-hour period, the cells are cultured at 37°C in MEM medium supplemented with 10% fetal bovine serum, 2mM glutamine, 10 U/ml penicillin and 10μg/ml streptomycin. The cells are serum-starved for 1-2 hours prior to the addition of stimulants.

[000310] For the assay, the cells are treated with medium alone or medium containing either a candidate agonist or 200 nM Phorbol ester- myristoyl acetate (*i.e.*, PMA, a positive control), and the cells are incubated at 37°C for varying times. To stop the reaction, the plates are placed on ice, the medium is aspirated, and the cells are rinsed with 1 ml of ice-cold PBS containing 1mM EDTA. Thereafter, 200μl of cell lysis buffer (12.5 mM MOPS, pH 7.3, 12.5 mM glycerophosphate, 7.5mM $MgCl_2$, 0.5mM EGTA, 0.5 mM sodium vanadate, 1mM benzamidine, 1mM dithiothreitol, 10 μg/ml leupeptin, 10 μg/ml aprotinin, 2μg/ml pepstatin A, and 1μM okadaic acid) is added to the cells. The cells are scraped from the plates and homogenized by 10 passages through a 23 3/4 G needle, and the cytosol fraction is prepared by centrifugation at 20,000 x *g* for 15 minutes.

[000311] Aliquots (5-10 μl containing 1-5 μg protein) of cytosol are mixed with 1 mM MAPK Substrate Peptide (APRTPGGRR (SEQ ID NO: 258), Upstate Biotechnology, Inc., N.Y.) and 50μM [γ-^{32}P]ATP (NEN, 3000 Ci/mmol), diluted to a final specific activity of ~2000 cpm/pmol, in a total volume of 25μl. The samples are incubated for 5 minutes at 30°C, and reactions are stopped by spotting 20μl on 2 cm^2 squares of Whatman P81 phosphocellulose paper. The filter squares are washed in 4 changes of 1% H_3PO_4, and the squares are subjected to liquid scintillation spectroscopy to quantitate bound label. Equivalent cytosolic extracts are incubated without MAPK substrate peptide, and the bound label from these samples are subtracted from

the matched samples with the substrate peptide. The cytosolic extract from each well is used as a separate point. Protein concentrations are determined by a dye binding protein assay (Bio-Rad Laboratories). Agonist activation of the receptor is expected to result in up to a five-fold increase in MAPK enzyme activity. This increase is blocked by antagonists.

H. [^{3}H]Arachidonic Acid Release

[000312] The activation of GPCRs also has been observed to potentiate arachidonic acid release in cells, providing yet another useful assay for modulators of GPCR activity. (*See, e.g.*, Kanterman *et al.*, Molecular Pharmacology 39:364-369 (1991).) For example, CHO cells that are stably transfected with a nGPCR-x expression vector are plated in 24-well plates at a density of 15,000 cells/well and grown in MEM medium supplemented with 10% fetal bovine serum, 2 mM glutamine, 10 U/ml penicillin and 10 μg/ml streptomycin for 48 hours at 37°C before use. Cells of each well are labeled by incubation with [^{3}H]-arachidonic acid (Amersham Corp., 210 Ci/mmol) at 0.5 μCi/ml in 1 ml MEM supplemented with 10mM HEPES, pH 7.5, and 0.5% fatty-acid-free bovine serum albumin for 2 hours at 37°C. The cells are then washed twice with 1 ml of the same buffer.

[000313] Candidate modulator compounds are added in 1 ml of the same buffer, either alone or with 10μM ATP and the cells are incubated at 37°C for 30 minutes. Buffer alone and mock-transfected cells are used as controls. Samples (0.5 ml) from each well are counted by liquid scintillation spectroscopy. Agonists which activate the receptor will lead to potentiation of the ATP-stimulated release of [^{3}H]-arachidonic acid. This potentiation is blocked by antagonists.

I. Extracellular Acidification Rate

[000314] In yet another assay, the effects of candidate modulators of nGPCR-x activity are assayed by monitoring extracellular changes in pH induced by the test compounds. (*See, e.g*, Dunlop *et al.*, Journal of Pharmacological and Toxicological Methods 40(1):47-55 (1998).) In one embodiment, CHO cells transfected with a nGPCR-x expression vector are seeded into 12 mm capsule cups (Molecular Devices Corp.) at 4 x 10^5 cells/cup in MEM supplemented with 10% fetal bovine serum, 2 mM L-glutamine, 10 U/ml penicillin, and 10 μg/ml streptomycin. The cells are incubated in this medium at 37°C in 5% CO_2 for 24 hours.

[000315] Extracellular acidification rates are measured using a Cytosensor microphysiometer (Molecular Devices Corp.). The capsule cups are loaded into the sensor chambers of the microphysiometer and the chambers are perfused with running buffer (bicarbonate-free MEM supplemented with 4 mM L-glutamine, 10 units/ml penicillin, 10 μg/ml streptomycin, 26 mM NaCl) at a flow rate of 100 μl/minute. Candidate agonists or other agents are diluted into the running buffer and perfused through a second fluid path. During each 60-second pump cycle, the pump is run for 38 seconds and is off for the remaining 22 seconds. The pH of the running

buffer in the sensor chamber is recorded during the cycle from 43-58 seconds, and the pump is re-started at 60 seconds to start the next cycle. The rate of acidification of the running buffer during the recording time is calculated by the Cytosoft program. Changes in the rate of acidification are calculated by subtracting the baseline value (the average of 4 rate measurements immediately before addition of a modulator candidate) from the highest rate measurement obtained after addition of a modulator candidate. The selected instrument detects 61mV/pH unit. Modulators that act as agonists of the receptor result in an increase in the rate of extracellular acidification compared to the rate in the absence of agonist. This response is blocked by modulators which act as antagonists of the receptor.

Example 12 - Using nGPCR-x proteins to isolate neurotransmitters

[000316] Isolated nGPCR-x proteins of the present invention can be used to isolate novel or known neurotransmitters (Saito *et al.*, Nature 400: 265-269, 1999). The cDNAs that encode the isolated nGPCR-x can be cloned into mammalian expression vectors and used to stably or transiently transfect mammalian cells including CHO, Cos or HEK293 cells. Receptor expression can be determined by Northern blot analysis of transfected cells and identification of an appropriately sized mRNA band (predicted size from the cDNA). Brain regions shown by mRNA analysis to express each of the nGPCR-x proteins could be processed for peptide extraction using any of several protocols ((Reinsheidk R.K. *et al.*, Science 270: 243-247, 1996; Sakurai, T., *et al.*, Cell 92; 573-585, 1998; Hinuma, S., *et al.*, Nature 393: 272-276, 1998). Chromotographic fractions of brain extracts could be tested for ability to activate nGPCR-x proteins by measuring second messenger production such as changes in cAMP production in the presence or absence of forskolin, changes in inositol 3-phosphate levels, changes in intracellular calcium levels or by indirect measures of receptor activation including receptor stimulated mitogenesis, receptor mediated changes in extracellular acidification or receptor mediated changes in reporter gene activation in response to cAMP or calcium (these methods should all be referenced in other sections of the patent). Receptor activation could also be monitored by co-transfecting cells with a chimeric $GI_{q/i3}$ to force receptor coupling to a calcium stimulating pathway (Conklin *et al.*, Nature 363; 274-276, 1993). Neurotransmitter mediated activation of receptors could also be monitored by measuring changes in [^{35}S]-GTPγS binding in membrane fractions prepared from transfected mammalian cells. This assay could also be performed using baculoviruses containing nGPCR-x proteins infected into SF9 insect cells.

[000317] The neurotransmitter which activates nGPCR-x proteins can be purified to homogeneity through successive rounds of purification using nGPCR-x proteins activation as a measurement of neurotransmitter activity. The composition of the neurotransmitter can be determined by

mass spectrometry and Edman degradation if peptidergic. Neurotransmitters isolated in this manner will be bioactive materials which will alter neurotransmission in the central nervous system and will produce behavioral and biochemical changes.

Example 13 - Using nGPCR-x proteins to isolate and purify G proteins

[000318] cDNAs encoding nGPCR-x proteins are epitope–tagged at the amino terminuus end of the cDNA with the cleavable influenza-hemagglutinin signal sequence followed by the FLAG epitope (IBI, New Haven, CT). Additionally, these sequences are tagged at the carboxyl terminus with DNA encoding six histidine residues. (Amino and Carboxyl Terminal Modifications to Facilitate the Production and Purification of a G Protein-Coupled Receptor, B.K. Kobilka , *Analytical Biochemistry*, Vol. 231, No. 1, Oct 1995, pp. 269-271). The resulting sequences are cloned into a baculovirus expression vector such as pVL1392 (Invitrogen). The baculovirus expression vectors are used to infect SF-9 insect cells as described (Guan, X. M., Kobilka, T. S., and Kobilka, B. K. (1992)*J. Biol. Chem.* **267**, 21995-21998). Infected SF-9 cells could be grown in 1000-ml cultures in SF900 II medium (Life Technologies, Inc.) containing 5% fetal calf serum (Gemini, Calabasas, CA) and 0.1 mg/ml gentamicin (Life Technologies, Inc.) for 48 hours at which time the cells could be harvested. Cell membrane preparations could be separated from soluble proteins following cell lysis. nGPCR-x protein purification is carried out as described for purification of the 5-2 receptor (Kobilka, Anal. Biochem., 231 (1): 269-271, 1995) including solubilization of the membranes in 0.8-1.0 %*n*-dodecyl -D-maltoside (DM) (CalBiochem, La Jolla, CA) in buffer containing protease inhibitors followed by Ni-column chromatography using chelating Sepharose™ (Pharmacia, Uppsala, Sweden). The eluate from the Ni-column is further purified on an M1 anti-FLAG antibody column (IBI). Receptor containing fractions are monitored by using receptor specific antibodies following western blot analysis or by SDS-PAGE analysis to look for an appropriate sized protein band (appropriate size would be the predicted molecular weight of the protein).

[000319] This method of purifying G protein is particularly useful to isolate G proteins that bind to the nGPCR-x proteins in the absence of an activating ligand.

[000320] Some of the preferred embodiments of the invention described above are outlined below and include, but are not limited to, the following embodiments. As those skilled in the art will appreciate, numerous changes and modifications may be made to the preferred embodiments of the invention without departing from the spirit of the invention. It is intended that all such variations fall within the scope of the invention.

[000321] The entire disclosure of each publication cited herein is hereby incorporated by reference.

What is claimed is:

1. An isolated nucleic acid molecule comprising a nucleotide sequence that encodes a polypeptide comprising an amino acid sequence homologous to sequences selected from the group consisting of: SEQ ID NO:129 to SEQ ID NO:257; said nucleic acid molecule encoding at least a portion of nGPCR-x.

2. The isolated nucleic acid molecule of claim 1 comprising a sequence that encodes a polypeptide comprising a sequence selected from the group consisting of SEQ ID NO:129 to SEQ ID NO:257.

3. The isolated nucleic acid molecule of claim 1 comprising a sequence homologous to a sequence selected from the group consisting of SEQ ID NO:1 to SEQ ID NO:128.

4. The isolated nucleic acid molecule of claim 1 comprising a sequence selected from the group of sequences consisting of SEQ ID NO:1 to SEQ ID NO:128.

5. The isolated nucleic acid molecule of claim 1 wherein said nucleic acid molecule is DNA.

6. The isolated nucleic acid molecule of claim 1 wherein said nucleic acid molecule is RNA.

7. An expression vector comprising a nucleic acid molecule of any one of claims 1 to 4.

8. The expression vector of claim 7 wherein said nucleic acid molecule comprises a sequence selected from the group of sequences consisting of SEQ ID NO:1 to SEQ ID NO:128.

9. The expression vector of claim 7 wherein said vector is a plasmid.

10. The expression vector of claim 7 wherein said vector is a viral particle.

11. The expression vector of claim 10 wherein said vector is selected from the group consisting of adenoviruses, baculoviruses, parvoviruses, herpesviruses, poxviruses, adeno-associated viruses, Semliki Forest viruses, vaccinia viruses, and retroviruses.

12. The expression vector of claim 7 wherein said nucleic acid molecule is operably connected to a promoter selected from the group consisting of simian virus 40, mouse mammary tumor virus, long terminal repeat of human immunodeficiency virus, maloney virus, cytomegalovirus immediate early promoter, Epstein Barr virus, rous sarcoma virus, human actin, human myosin, human hemoglobin, human muscle creatine, and human metalothionein.

13. A host cell transformed with an expression vector of claim 7.

14. The transformed host cell of claim 13 wherein said cell is a bacterial cell.

15. The transformed host cell of claim 14 wherein said bacterial cell is E. coli.

16. The transformed host cell of claim 13 wherein said cell is yeast.

17. The transformed host cell of claim 16 wherein said yeast is S. cerevisiae.

18. The transformed host cell of claim 13 wherein said cell is an insect cell.

19. The transformed host cell of claim 18 wherein said insect cell is S. frugiperda.

20. The transformed host cell of claim 13 wherein said cell is a mammalian cell.

21. The transformed host cell of claim 20 wherein mammalian cell is selected from the group consisting of chinese hamster ovary cells, HeLa cells, African green monkey kidney cells, human HEK-293 cells, and murine 3T3 fibroblasts.

22. An isolated nucleic acid molecule comprising at least 10 nucleotides, said nucleic acid molecule comprising a nucleotide sequence complementary to at least a portion of a sequence selected from the group of sequences consisting of SEQ ID NO:1 to SEQ ID NO:128.

23. The nucleic acid molecule of claim 22 wherein said molecule is an antisense oligonucleotide directed to a region of a sequence selected from the group of sequences consisting of SEQ ID NO:1 to SEQ ID NO:128.

24. The nucleic acid molecule of claim 23 wherein said oligonucleotide is directed to a regulatory region of a sequence selected from the group of sequences consisting of SEQ ID NO:1 to SEQ ID NO:128.

25. A composition comprising a nucleic acid molecule of any one of claims 1 to 4 or 22 and an acceptable carrier or diluent.

26. A composition comprising a recombinant expression vector of claim 7 and an acceptable carrier or diluent.

27. A method of producing a polypeptide that comprises a sequence selected from the group of sequences consisting SEQ ID NO:129 to SEQ ID NO:257, and homologs thereof, said method comprising the steps of:

a) introducing a recombinant expression vector of claim 8 into a compatible host cell;

b) growing said host cell under conditions for expression of said polypeptide; and

c) recovering said polypeptide.

28. The method of claim 27 wherein said host cell is lysed and said polypeptide is recovered from the lysate of said host cell.

29. The method of claim 27 wherein said polypeptide is recovered by purifying the culture medium without lysing said host cell.

30. An isolated polypeptide encoded by a nucleic acid molecule of claim 1.

31. The polypeptide of claim 30 wherein said polypeptide comprises a sequence selected from the group of sequences consisting of SEQ ID NO:129 to SEQ ID NO:257.

32. The polypeptide of claim 30 wherein said polypeptide comprises an amino acid sequence homologous to a sequence selected from the group of sequences consisting of SEQ ID NO:129 to SEQ ID NO:257.

33. The polypeptide of claim 30 wherein said sequence homologous to a sequence selected from the group of sequences consisting of SEQ ID NO:129 to SEQ ID NO:257 comprises at least one conservative amino acid substitution compared to the sequences in the group of sequences consisting of SEQ ID NO:129 to SEQ ID NO:257.

34. The polypeptide of claim 30 wherein said polypeptide comprises an allelic variant of a polypeptide with a sequence selected from the group of sequences consisting of SEQ ID NO:129 to SEQ ID NO:257.

35. A composition comprising a polypeptide of claim 34 and an acceptable carrier or diluent.

36. An isolated antibody which binds to an epitope on a polypeptide of claim 30.

37. The antibody of claim 36 wherein said antibody is a monoclonal antibody.

38. A composition comprising an antibody of claim 36 and an acceptable carrier or diluent.

39. A method of inducing an immune response in a mammal against a polypeptide of claim 30 comprising administering to said mammal an amount of said polypeptide sufficient to induce said immune response.

40. A method for identifying a compound which binds nGPCR-x comprising the steps of:

a) contacting nGPCR-x with a compound; and

b) determining whether said compound binds nGPCR-x.

41. The method of claim 40 wherein the nGPCR-x comprises an amino acid sequence selected from the group consisting of SEQ ID NO:129 to SEQ ID NO:257.

42. The method of claim 40 wherein binding of said compound to nGPCR-x is determined by a protein binding assay.

43. The method of claim 40 wherein said protein binding assay is selected from the group consisting of a gel-shift assay, Western blot, radiolabeled competition assay, phage-based expression cloning, co-fractionation by chromatography, co-precipitation, cross linking, interaction trap/two-hybrid analysis, southwestern analysis, and ELISA.

44. A compound identified by the method of claim 40.

45. A method for identifying a compound which binds a nucleic acid molecule encoding nGPCR-x comprising the steps of:

a) contacting said nucleic acid molecule encoding nGPCR-x with a compound; and

b) determining whether said compound binds said nucleic acid molecule.

46. The method of claim 45 wherein binding is determined by a gel-shift assay.

47. A compound identified by the method of claim 45.

48. A method for identifying a compound which modulates the activity of nGPCR-x comprising the steps of:

a) contacting nGPCR-x with a compound; and

b) determining whether nGPCR-x activity has been modulated.

49. The method of claim 48 wherein the nGPCR-x comprises an amino acid sequence selected from the group consisting of SEQ ID NO:129 to SEQ IDNO:257.

50. The method of claim 48 wherein said activity is neuropeptide binding.

51. The method of claim 48 wherein said activity is neuropeptide signaling.

52. A compound identified by the method of claim 48.

53. A method of identifying an animal homolog of nGPCR-x comprising the steps:

a) comparing the nucleic acid sequences of the animal with a sequence selected from the group of sequence consisting of SEQ ID NO:1 to SEQ ID NO:128, and portions thereof, said portions being at least 10 nucleotides; and

b) identifying nucleic acid sequences of the animal that are homologous to said sequence selected from the group sequence consisting of SEQ ID NO:1 to SEQ ID NO:128, and portions thereof, said portions comprising at least 10 nucleotides.

54. The method of claim 53 wherein comparing the nucleic acid sequences of the animal with a sequence selected from the group of sequences consisting of SEQ ID NO:1 to SEQ ID NO:128, and portions thereof, said portions being at least 10 nucleotides, is performed byDNA hybridization.

55. The method of claim 53 wherein comparing the nucleic acid sequences of the animal with a sequence selected from the group of sequences consisting of SEQ ID NO:1 to SEQ ID NO:128, and portions thereof, said portions being at least 10 nucleotides, is performed by computer homology search.

56. A method of screening a human subject to diagnose a disorder affecting the brain or genetic predisposition therefor, comprising the steps of:

(a) assaying nucleic acid of a human subject to determine a presence or an absence of a mutation altering an amino acid sequence, expression, or biological activity of at least one nGPCR-x that is expressed in the brain, wherein the nGPCR-x comprises an amino acid sequence selected from the group consisting of SEQ ID NO:129 to SEQ ID NO:257, and allelic variants thereof, and wherein the nucleic acid corresponds to a gene encoding the nGPCR-x; and

(b) diagnosing the disorder or predisposition from the presence or absence of said mutation, wherein the presence of a mutation altering the amino acid sequence, expression, or biological activity of the nGPCR-x in the nucleic acid correlates with an increased risk of developing the disorder.

57. A method according to claim 56, wherein the disease is a mental disorder.

58. A method according to claim 56, wherein the assaying step comprises at least one procedure selected from the group consisting of:

a) comparing nucleotide sequences from the human subject and reference sequences and determining a difference of at least a nucleotide of at least one codon between the nucleotide sequences from the human subject that encodes a nGPCR-x reference sequence;

(b) performing a hybridization assay to determine whether nucleic acid from the human subject has a nucleotide sequence identical to or different from one or more reference sequences;

(c) performing a polynucleotide migration assay to determine whether nucleic acid from the human subject has a nucleotide sequence identical to or different from one or more reference sequences; and

(d) performing a restriction endonuclease digestion to determine whether nucleic acid from the human subject has a nucleotide sequence identical to or different from one or more reference sequences.

59. A method according to claim 58 wherein the assaying step comprises: performing a polymerase chain reaction assay to amplify nucleic acid comprising nGPCR-x coding sequence, and determining nucleotide sequence of the amplified nucleic acid.

60. A method of screening for an nGPCR-x hereditary mental disorder genotype in a human patient, comprising the steps of:

(a) providing a biological sample comprising nucleic acid from said patient, said nucleic acid including sequences corresponding to alleles of nGPCR-x; and

(b) detecting the presence of one or more mutations in the nGPCR-x allele;

wherein the presence of a mutation in a nGPCR-x allele is indicative of a hereditary mental disorder genotype.

61. The method according to claim 60 wherein said biological sample is a cell sample.

62. The method according to claim 60 wherein said detecting the presence of a mutation comprises sequencing at least a portion of said nucleic acid, said portion comprising at least one codon of said nGPCR-x allele, said portion comprising at least 10 nucleotides.

63. The method according to claim 60 wherein said nucleic acid is DNA.

64. The method according to claim 60 wherein said nucleic acid is RNA.

65. A kit for screening a human subject to diagnose a mental disorder or a genetic predisposition therefor, comprising, in association:

(a) an oligonucleotide useful as a probe for identifying polymorphisms in a human nGPCR-x gene, the oligonucleotide comprising 6-50 nucleotides in a sequence that is identical or complementary to a sequence of a wild type human nGPCR-x gene sequence or

nGPCR-x coding sequence, except for one sequence difference selected from the group consisting of a nucleotide addition, a nucleotide deletion, or nucleotide substitution; and

(b) a media packaged with the oligonucleotide, said media containing information for identifying polymorphisms that correlate with mental disorder or a genetic predisposition therefor, the polymorphisms being identifiable using the oligonucleotide as a probe.

66. A method of identifying a nGPCR-x allelic variant that correlates with a mental disorder, comprising the steps of:

(a) providing a biological sample comprising nucleic acid from a human patient diagnosed with a mental disorder, or from the patient's genetic progenitors or progeny;

(b) detecting in the nucleic acid the presence of one or more mutations in an nGPCR-x that is expressed in the brain, wherein the nGPCR-x comprises an amino acid sequence selected from the group consisting of SEQ ID NO:129 to SEQ ID NO:257, and allelic variants thereof, and wherein the nucleic acid includes sequence corresponding to the gene or genes encoding nGPCR-x;

wherein the one or more mutations detected indicates an allelic variant that correlates with a mental disorder.

67. A purified and isolated polynucleotide comprising a nucleotide sequence encoding a nGPCR-x allelic variant identified according to claim 66.

68. A host cell transformed or transfected with a polynucleotide according to claim 67 or with a vector comprising the polynucleotide.

69. A purified polynucleotide comprising a nucleotide sequence encoding nGPCR-x of a human with a mental disorder;

wherein said polynucleotide hybridizes to the complement of a sequence selected from the group consisting of SEQ ID NO:1 to SEQ ID NO:128 under the following hybridization conditions:

(a) hybridization for 16 hours at 42°C in a hybridization solution comprising 50% formamide, 1% SDS, 1 M NaC1, 10% dextran sulfate and

(b) washing 2 times for 30 minutes at 60°C in a wash solution comprising 0.1x SSC and 1% SDS; and

wherein the polynucleotide that encodes nGPCR-x amino acid sequence of the human differs from the sequence selected from the group consisting of SEQ ID NO:1 to SEQ ID NO:128 by at least one residue.

70. A vector comprising a polynucleotide according to claim 69.

71. A host cell that has been transformed or transfected with a polynucleotide according to claim 69 and that expresses the nGPCR-x protein encoded by the polynucleotide.

72. A host cell according to claim 71 that has been co-transfected with a polynucleotide encoding the nGPCR-x amino acid sequence set forth in a sequence selected from the group consisting of SEQ ID NO:1 to SEQ ID NO:128 and that expresses the nGPCR-x protein having the amino acid sequence set forth in SEQ ID NO:129 to SEQ ID NO:257.

73. A method for identifying a modulator of biological activity of nGPCR-x comprising the steps of:

a) contacting a cell according to claim 72 in the presence and in the absence of a putative modulator compound;

b) measuring nGPCR-x biological activity in the cell;

wherein decreased or increased nGPCR-x biological activity in the presence versus absence of the putative modulator is indicative of a modulator of biological activity.

74. A method to identify compounds useful for the treatment of a mental disorder, said method comprising the steps of:

(a) contacting a composition comprising nGPCR-x with a compound suspected of binding nGPCR-x;

(b) detecting binding between nGPCR-x and the compound suspected of binding nGPCR-x;

wherein compounds identified as binding nGPCR-x are candidate compounds useful for the treatment of a mental disorder.

75. A method for identifying a compound useful as a modulator of binding between nGPCR-x and a binding partner of nGPCR-x comprising the steps of:

(a) contacting the binding partner and a composition comprising nGPCR-x in the presence and in the absence of a putative modulator compound;

(b) detecting binding between the binding partner and nGPCR-x;

wherein decreased or increased binding between the binding partner and nGPCR-x in the presence of the putative modulator, as compared to binding in the absence of the putative modulator is indicative a modulator compound useful for the treatment of a mental disorder.

76. A method according to claim 74 or 75 wherein the composition comprises a cell expressing nGPCR-x on its surface.

77. A method according to claim 76 wherein the composition comprises a cell transformed or transfected with a polynucleotide that encodes nGPCR-x.

78. A method of purifying a G protein from a sample containing said G protein comprising the steps of:

a) contacting said sample with a polypeptide of claim 1 for a time sufficient to allow said G protein to form a complex with said polypeptide;

b) isolating said complex from remaining components of said sample;

c) maintaining said complex under conditions which result in dissociation of said G protein from said polypeptide; and

d) isolating said G protein from said polypeptide.

79. The method of claim 78 wherein said sample comprises an amino acid sequence selected from the group of sequences consisting of SEQ ID NO:129 to SEQ ID NO:257.

80. The method of claim 78 wherein said polypeptide comprises an amino acid sequence homologous to a sequence selected from the group of sequences consisting of SEQ ID NO:129 to SEQ ID NO:257.

81. The method of claim 78 wherein said polypeptide comprises an amino acid sequence selected from the group consisting of: SEQ ID NO:129 to SEQ ID NO:257.

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tggcgagaag acatatcaag ctttggaggc actgatagga gaccaatgga gctgcttcac 180

ggagagacac atgagtgagg ctggaaaggg aggaaggggc aggccagcag ggtcttgtag 240

gacacttagg agtttggtct ttacaatatt gacagttggc aatttttga ttattttaag 300

caggatgaag acatgatcag atttgagttt caaaagctca ctcactgcag tgttagaatg 360

agttgggtta aattttctca tctgaaacat aaggatggat acacttgccc tgtgtattga 420

acaggtcatt gtgtaatcag tgatcacaca agatttatac aaggtgcata gaagtgtttt 480

atgaaatata aatgctatag aaaattacac agcaatattt tacaggaagc aataccacca 540

gatggtcata ttctttcaag ttttttctgt gaacaaaggc agtctgaact cataaaat 598

<210> 9
<211> 644
<212> DNA
<213> Homo sapiens

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aagtgcacac ctattcaaaa ttgcaagtga tatctctttt gtactgattt agcctgtacc 360

tgaaagcaat agccatacac atgagtatac tgaattaagt gcactagtag atgactttct 420

ataagaaaga gggggaaaca cccaaattac attcaaagac attactggaa attaattatg 480

tataattccc agtataatgc aaacatttat cctcgcgtta tccagtttct aactgtagga 540

gaaattgcat ttattcctta aaatttaaca ctactacgct taaaacaaaa agtcatgcta 600

gtatgcatat ttccacaaat cttataaaat agatgatatt ttca 644

<210> 10
<211> 668
<212> DNA
<213> Homo sapiens

<400> 10
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tccacccctc ctccctcccc aaagctacca cagcttactt gagaataaca acaatatcat 180

gtgaccctta catagcaatg gtcaatttat ccattgatct ctactatata atgggattgt 240

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gagaggtcac ctgtgatggt cacatacctg gctccatgta cactatttcc ctcctgggcc 360

tttgccatac tgtgctgagc tgcagttggg gaaatatctc agggacgtgc ctcatcaggg 420

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aagtgccact cagaacactg gccctgaccc taaagaatca attagtggtc tgcctgcagc 540

gaaactgttt tcaaggccct tttagtgctc tcacattcca ccaggtatcc cccttggccc 600

catgagcttg acagtcttcc aaaatatttc tgacaacccc agtgagtgat gttcaccaga 660

tgctgatc 668

<210> 11
<211> 502
<212> DNA
<213> Homo sapiens

<400> 11
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agggatggga cttttctctg cagcctacct agatcatggt actcacaagc cttgttctcg 120

caggcctcac ctgcttttca gcccggggcg ccctgggcaa ccagagtgca gaggacacgt 180

gttcatcagt cttcaccccg tactggcaac tttcttggtg caatgccctt gactgggcac 240

tgggaaggct gtaaaatcag tcttcacccc gtactgggaa ctttcttggt gcaatgccct 300

tgactgggca ctgggaaggc tgtaaaaaca gtttctgccc ccaagaggag caaagggtgg 360

gcttgcaccc agataactgc cccacaaatg gcatgtgctg aagacctggg ggcgcaggtg 420

ctgtggccct catgcttttc cccgtgctcc tggaaggagg ctcaatgcct tggcgccagc 480

ttcatggttc ttggggctcc tg 502

<210> 12
<211> 609
<212> DNA
<213> Homo sapiens

<400> 12
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agcaggggtg agtgtcggaa gtcttgctgt ccacagccat cctcaactcc ccaaacctgc 120

aaccagggcc gctcagcttt catgagctta cctcccagcc tctttttag tgctgccttt 180

ggagaaagaa tgacgtggtc aaaaccttg aaaatcagga tttaaacaat aaattttaaa 240

tataagcaag atgctttcct ataggaaaaa aagaatacat gaacgaaatt cagctttcta 300

catctgcaaa ttcaactgat agtgaattta aagggccatt tcctgccctg taatgatcac 360

tgatgacatt gacaggctgc ttctctcttt cttggctgca cctcatgggg gcatcctggc 420

acctgctttg tggtcagggt gtagagaaga ccccccagc tgtcaactct ttaactgtca 480

acatctgcgt caacatctgc ttagaggatc ttagtcacac accaacaatt cttacttaaa 540

atataaaggg ccacggggat gagtctttga actctgcgcc ctcccttccc ttgcaaggcc 600

aaatgtgta 609

<210> 13
<211> 1000
<212> DNA
<213> Homo sapiens

<400> 13
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aaaaaattga gtattgaaat tggctgttgc atcagtgaag aaaagcaaca tccctaccac 120

ccctcaaaag agacattaaa gtagttggat taagggcacg ggagtatttg ctttccgatt 180

tagtgataat gtgagtgctt aatgaaatga ctaacacatt ccctgattat agagctggtc 240

agtggatctt gctgagtttc ctgtggacct atgtgaaatg atcggcatct gttcagggtt 300

tactaggtgc taagcacctt tacatgtgac atccattgaa tgctcacaac acccccagga 360

aattggtacc agtgttatcc tcatggtaca gtgaaggata ctgagactta ggttgcatag 420

cctgcaggtt ggacacactt ctttctgact gctggggagc tgtgctttta accactgctg 480

atccggcttg ttttccccag atgcaggcct ggggtagtct cctttctgga ctgagaagag 540

aagaatggag aagcccctct tcccattgtg agtagacagt aaatggttag agagtagcca 600

ggagcttctg gaaaccagag ttcctttcct cagctgaaaa gaaccctaag agtagactgc 660

ctgggatggc gtgcgggatg ggaggatcac tggacctgtg ggccagaaac ttgggtttga 720

gtcccagctc tagctttgct tagttgtgtg actctcagaa agtcatccaa cctctgtggt 780

gcttattttc agtgatagta cctgtgggca cataggacct gtggggaatg attacctttt 840

agccccatcc tatgacaata tggtttgttt ttaaatccag gttagcactg acttctcact 900

gacttctctt gtgttttcag agtgcctttg cattggtttg gctttggcta cacagcactg 960

gttgtttctg gtgggatcgt tggctatgta aaaacaggta 1000

<210> 14
<211> 1000
<212> DNA
<213> Homo sapiens

<400> 14
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atcttttctt tttgggacaa gcttcagccc tgctttttga gtcttcccac tgattgaatc 180

agtcctaccc ataatataca aacataaatc ctgaattttt tttagactta ccaaattcaa 240

ctggttgtgg actgaattac atctgcaaaa ggtcatcaca gaaacagctg gattatcatt 300

tgattgagta actgggggct atagcctagc caagttaaca tatcaaagtc actgcagatg 360

ggtgagttga ataaaatctt taccaaagat gatgcttaga atgcattcca acaaaagttt 420

taatatttaa tgacagaaaa ggaaatatta tacataccta aaagcttcct ccctactgta 480

ttaaactctc caccaaagga ttttctgaag gaaacacttg aaggtattga tgacaactgt 540

ataaataaaa gagttattct gattattatt gagagatata atgctcattt tatttattac 600

atttggagag ctctaaataa gtttgtaatt atggcctgta aaagaaaaaa gtgttaattt 660

ccttttaaat ggacaactaa gatttttta taatattgaa ctcattaggc caaaacatgc 720

attcattttg ggattattta aatgaattaa ttcattcaac agatatataa ttgaaacata 780

gtatacagaa gacattgtgc tagattctgg cgataaaatg gtgaataaaa ccaagactgc 840

ccctcccttc aagaatttta tgatttagtc atggaaaaaa tacattaatc aaatattgac 900

acgaaaaaat tatcacaaac tgcgataatt cgtgatagta tagttgcaat gagtctatgt 960

tcaatgattc ttgatttttt ctgtgtgtta gaaagcttac 1000

<210> 15
<211> 1000
<212> DNA
<213> Homo sapiens

<400> 15
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atctagcttt accttattca ctgagttttt taaataaata tttgaatttc tatgtgacat 180

ttaaacattt cctatgtaat ttgctgtaac taacttgaca tactgaaatt ttacttaaag 240

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ttagattcta agattatctt ttcgtatttg cttttctctt tctctgcatg ttgatttcca 480

tcacaccatt tgaagttaag tttccaagta actgacagag atagaaatga aatagtggtt 540

atttttagtg aattgggagg ggcacaggag aaccctctaa agcatcagga aatgtcctac 600

atcttaatct acatggtagt tacacatgta aaaactctga gcgatatact tcagatttgt 660

accctctact gtgtataagt tccatctcaa aaaagcgtgg gtttgcgggg gaagttgcag 720

tcatcctaac actttactcc taaatactta tacatgtaat tcctaagaac aaggacattc 780

tcctatataa ttacgttacc atcctcacat ttaagaacgt taattccata acaatatgta 840

gtattcaatc aatgttaaaa atttcccaag tcccaagaat gattcttccc ccctcaggat 900

tacacactgc atttggttgt tatgtgcact tggtcttgta cagtgtggaa taatccccaa 960

ccttttttatt gtccaagaca ttaacttatc aaggagtcta 1000

<210> 16
<211> 630
<212> DNA
<213> Homo sapiens

<400> 16
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cgagcggatg gcatggaggc tggagagcca ggcaggggtc aaagtccccg tgcaaggagc 180

ttggctgtca ttccatgggc tactggagag agaagccgtg gagcaatggg atccgatgtt 240

aacttgaaag agatcactct tactcaccag tgaaactgag tgaactactc acatgctcag 300

ccatttaatg gatctagagg gaattatgca gagtgagaaa agccaatccc aaaaggttat 360

atacagcatt gattccattt acacgacact gttgaaatga cattgcagaa atgaagaaca 420

gattagtggt tgctggtagt taaggagggg tagaagcatc cggacggtgg ttatgaaaag 480

ccaacacagg gatccctgtg gtaataaagc cgttctgtaa cttccttgac tttgtcaatg 540

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ggttaaaggg tatactcttc atattatttc 630

<210> 17
<211> 314
<212> DNA
<213> Homo sapiens

<400> 17
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attttttttc agtgcatttg tatcttctaa ttttctcata gtaatatcac agggtcccca 180

taggtgatgc tgaatatggg caactggttt tttttgtttt ttttttttta cctgttgtct 240

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cctgttagga acga 314

<210> 18
<211> 181
<212> DNA
<213> Homo sapiens

<400> 18
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aatcccgatg aggttacagg acacaaaaga taacatgagt catcaccgaa taagactagg 120

aggccttccg gaaagggaca attgggggaa aagcttgcca aaactcttca ttaaacacag 180

t 181

<210> 19
<211> 594
<212> DNA
<213> Homo sapiens

<400> 19
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gcctgccagg aaagtttctg acccttgcct ttgacctcct gttgctactg tccattgtgg 120

tcagcatgcc tcacctagtc atctacttct tggctgagta actctacagg aagaggcaca 180

gggagtccct aaaggctgtt tttcagaggg ctttgttgag tgagatggag gcatggataa 240

aatgaggcgt ttcaggcccc cgatcccagg gcagatttca gcctcacagc tggaaacaaa 300

ctgctcttct agggggctca gctcctccac aaaggcaggg actgcctatg cacaaggctg 360

taaaagggat catgtctgga aaacatgctg aatcctccaa ggagcagggt gaatgttctt 420

gagattattt attacctttg tgtattttca gagtaaccag atttctgact gaattcaaga 480

caaaattact ttgcttctgt tgatagccca ttattctcaa ttcccatgga aaccctctgg 540

aaaggcaggt caggagcaaa gcagaccttc ctggcttctt ctttttttt tttt 594

<210> 20
<211> 391
<212> DNA
<213> Homo sapiens

<400> 20
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agctgttttt atgtaggcca cattctcata cctcccttcc caacacagag aacagtataa 120

cagaatactg ggaacacaat taggaaatga aattagaaaa agggagcatc aggtaaagca 180

agcatttaaa gaagccaaaa aggctttctc ctaacaagag gcacaaacgc gtgtgagcgg 240

ccggcgagtc cgagctgcac tgcggggccg ctaccttcag acttccctgt acgctccaca 300

cttccacaac gggcgaggct acttttataa tcataaaaaa tgcccaatca atacaatttt 360

caaaagaaga agcggaaggg aaaaaccaat c 391

<210> 21
<211> 363
<212> DNA
<213> Homo sapiens

<400> 21
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tgccagcttt actgatcgag gattggatta tattttaaac atatcatggc gttggttcca 120

aaacaatggt caaagcagct tgccaaaaaa aaaataccaa gagggatata tcctgattga 180

ttctcacatt cctctcagat acattggtaa atgtgatata ctggtcctat aaatgtactg 240

aacaacgtgt gacagaaacc aggcagggac attcctgaag gcaggttgcc gcagctgtct 300

atagccacat acctgatatg caacaatctg cattcattct gattgtatca ggtgaaagct 360

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<210> 22
<211> 731
<212> DNA
<213> Homo sapiens

<400> 22
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gaagaggtac ctggattttg gagtcaaaca aaccttgatt ctctcatttc ctagttgggt 180

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aatatttagt atatactaag tgctcaataa atgctactgc tatttgctcc tctcatccta 360

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atgagcatcg accgtggagc cggtcaataa aagacagcaa aggcttctcc tctggccacc 480

ccttccccat gtgttggccc aatcatgtcc cactttggtc ctcaaggtta tagtatgggc 540

tgttcaattc cacaaaggcc caagttaata tctgaccaac cccaagtaat taaatgagta 600

ctggccctgt tggcaactct gttgctggac aggccttgtg ttcagtttca gcgcatggac 660

tgagcacgca ccctgatcag ccccccgtgc tcactgcttt cttacatcaa atcctcacaa 720

gcaaccaccc g 731

<210> 23
<211> 624
<212> DNA
<213> Homo sapiens

<400> 23

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tttccagcct tatctgagaa gttgaagtgg ggggtagggg acactcctgc tgccaactgc 180

ccgcactcac cagtgatgag gttgtccaaa gggttggtgg gcatgcagaa gatgcccacc 240

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gcataggcca caatgaacat ggccgccaca ggggaggtgt gctgatagta ggaggagaag 420

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ccatgccctg gtcccccaag catg 624

<210> 24
<211> 555
<212> DNA
<213> Homo sapiens

<400> 24
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gaaatttctt ccccagtgta gtagtgttgg gaggtgggac ctagttgggg aatggcttgg 180

tgccactctc taggtagtgg ctgagttctt gctgtggcga gaatgaatta gttcttgcgg 240

gaatgaattc ttaatagttc ctgccagagt gagtttttat aaagccagga tgccccttgg 300

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gcatgagacc ttcaccagaa gccaagtaga tgtcagcacc gtgcttctct aactttccac 420

ctgcaaaact gtgagctaaa taaacctctt ttctttataa attacctagc ctctgtattc 480

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<210> 25
<211> 776
<212> DNA
<213> Homo sapiens

<400> 25
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gcatgcaagc ccaagaggcc tgtagtactg catcccacat gctttctttt cgtttggttt 180

ggttacatgt tctgtcttgg aattaactgt ttattgtaca atcttcctgg atccttgagc 240

attttgccct tgcatccaaa attgggcagc ctcaaccctt acatcaagtt tatttcacct 300

gtaaactctg ctagcatttt aatttttact gcttttctga gtgctgcgct tatcaagttc 360

aatatatttg aagtggacta ccctttacct tatttccccc ccaccacaaa agccctgcaa 420

cttttactgt agtattctgc tgaacacagg tgggaacaca gatgtcatat tacagcagaa 480

atatctattc ttgtgaggac acatcctgac agtgacatga agtgacacat tgtgcatacc 540

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ccaagctaag ggtggcgggt gctagacagc tcgctaagcc ccctgccaac tcccttccat 660

gtacctgctt cacaacacga agctgcttca caacagtgcc aacgaacaac tgatcgacca 720

aggacaaatc actgaattca tccgtggaag cgaagctctg tgtactacat gtaaag 776

<210> 26
<211> 651
<212> DNA
<213> Homo sapiens

<400> 26
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tgtacaggta aggtgtaatc aagtttgctt acaaaatttt tttaaactat gaccttggca 180

gagatgtagt tgtaatagaa attatattct ggaactgtaa aagcaactaa atgtataatt 240

atttggctgt tcttcctgct ctttctctga ctcttcccat atctggatcc ttcttactca 300

ttggatttca ggacaaaaaa tgctttctca gagatggctt ttgtgttcat ctgtttaaac 360

gcagtcccct ttcttagtct tgtcatcttc taacaaatta ccatgtttac tcattgctat 420

ggtttggata tggtttgctt gtccccacca aatcttatgt tgaaataatg atctccagag 480

tggtggtatt gggaggtggg gcctagtgag aggtgttggc atcatggggg cagatccctt 540

gtaaatggct tggtgccatt ctcatgggag tgaatgagtt cttgctcttt tgagactggg 600

ttgcttcttg agggaaaggg attagtctcc ctccgagtgg gttggtataa a 651

<210> 27
<211> 362
<212> DNA
<213> Homo sapiens

<400> 27
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tcttattaaa gcaaggctgt agaggccagg tcacattctt tccatgacat tttaatgagc 180

agtttaggga gggtggttgg cgtggtgatt gtaagtgggg acaagtggca aagattaact 240

cagtattcat tttgcctgac tgcagaattt aaataaccct tccacttgtt gctggtactg 300

tcaacacgtg gtagaaaata taaattagat tgtgctctac acagactgta tataataatt 360

tc 362

<210> 28
<211> 557
<212> DNA
<213> Homo sapiens

<400> 28
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aagacattca taaacgatcc actcccacaa cccaaacagc tcccaccagg ccgtacctcc 240

aatactaggt gggcatcaaa ttccaacatg aaacttggtg gggccacaca aaccatatcc 300

gaaccatagc aaatgtcttg aaggtaagaa ttctctacca caagcttctc tgctgggtac 360

atatgtcctg cccataagca aatcttgggt gagcactggt gactaaccag catcacagaa 420

agaaaagaca gataccaggg ccctgttacc aacagcctgg caaatagatg accacactgg 480

atctcaattt acaaaatggg ggtaaccagg tggcctagat aaatcttgat agatatacag 540

agagaggtaa agtagtg 557

<210> 29
<211> 609
<212> DNA
<213> Homo sapiens

<400> 29
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tggggaaagt gagtcaaaat tctgggaagc agcaaagcaa ttatccaagc tggaattaaa 180

gcctagcgtt ctaaatgctc atttagtgct agtgctaccc aaaatgattc tacattttat 240

aagcaggtaa taaataaata aatataagca ggatcagcca ggatgaagtg aaaataaaaa 300

taattccatg gagttttaac agcttttctg taacttttga ctgcagctct ttgcctgaag 360

tgtaacatac aaaaccaaaa gagagtaaaa cagagcatac tgaaatcttg acacctctca 420

aagaactaga tggtttaccc ttttacatag gaagcaaata aaggagaaac tgtcaatgac 480

tgatgggaac acagtacaaa atttaagtta gtggtttatt tttaaagctt gtataatatg 540

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<210> 30
<211> 689
<212> DNA
<213> Homo sapiens

<400> 30

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ggtgccaggc tcttttcaac aaccagttct tgcaagaatt cactctcatg agtatggcac 180

caagacattc ataaacgatc cactcccaca acccaaacag ctcccaccag gccgtacctc 240

caatactagg tgggcatcaa attccaacat gaaacttggt ggggccacac aaaccatatc 300

cgaaccatag caaatgtctt gaaggtaaga attctctacc acaagcttct ctgctgggta 360

catatgtcct gcccataagc aaatcttggg tgagcactgg tgactaacca gcatcacaga 420

aagaaaagac agataccagg gccctgttac caacagcctg gcaaatagat gaccacactg 480

gatctcaatt tacaaaatgg gggtaaccag gtggcctaga taaatcttga tagatataca 540

gagagaggta aagtagtgaa agccctatga aaaatgtaat tcaatatgaa aacgtatggt 600

attattacta caatgctaat aagcaattaa atgtttctca aaaataggga agactgggaa 660

gaagggaagc attacaagct aagctggct 689

<210> 31
<211> 490
<212> DNA
<213> Homo sapiens

<400> 31
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gtggatttct atatcttcct cttcaaactc accgtcactc tagagaaaga actcttcttt 180

cctgtgtttt atttatgtct aaaacatagg taaacggtgt atgtatgatg tcttcttctt 240

atttatttcc ttttgttcta attgcaaaaa atcacacatg ttccttgtaa aaaaatcaac 300

caaccaacca accttgaaaa acttaaacaa tgaacaaaga gaaaagaaat tacctaacat 360

caaacataat gtgtatacat tacaaaagct tgaaaaatac agaaaaacac aaaggaaaga 420

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<210> 32
<211> 634
<212> DNA
<213> Homo sapiens

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ggaaagaaat taaagctgct acaactagac agtcagaagt tgctcagaag tggtagtcct 180

aaatgttctt aagggagcta ctctggtttg gttatggttt gtctgtcccc accaaacctc 240

atgttgacat tttcttccca gtgtggcagt gttgagaggt gaggcctagt gggaggtgtc 300

tgggtcatgg aggtggatcc ctcatgaaca cttagtgctg ctctcaagtt agtgagttct 360

agctttggca agactgaatt agttcttgtg gaaatggagt agtttcctcg agagtgggct 420

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tctggcagca cagaagcctc accagaagct gagcagatgc tggcaccatg gttcttatac 540

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<210> 33
<211> 602
<212> DNA
<213> Homo sapiens

<400> 33
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taaggagtgg tctggtcatg atagactttg gaatctattt gaggtgaagt tggaagtttt 120

gaagaatttt aaccaagcca atggattttt attatttata cttattaaag attattttga 180

ctgcagtgtg gagaatagag tagaaagaaa tagagaagta aggaacctac tgctatttca 240

catgaaaatg atgtatcatt aatgtctttt atctgcatgg gggctatgca gggagaagtg 300

gccaaatata agatataaac gggagtatac atgccaggac ttgttgatgg attacatact 360

agtgttaata gttaaccttc agttcttgaa tggggaactt ttacttatgt atgcagtatt 420

tatacattat tctagatgtg tttgactaca aatgacagaa atttaattaa aatgcaattt 480

gataaagaat ttactcataa gtcatattgt ctcatatgac tgggaaatct aagggtgagt 540

taggacttta ggaaaagctg tatcccaagc ctatagatga cttctgaact tagtattaat 600

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<210> 34
<211> 238
<212> DNA
<213> Homo sapiens

<400> 34
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ccccccgccc agttcagcaa ctataagaaa ccatggctgg ccgaatcaga ggccgaaggg 120

cttactgttc taagactttt ggaactatct gttttatccc ctacttttc caactacatt 180

gtgtattact cctactggtg taaatattta ccaaagaaaa ttttttcact ttaatatc 238

<210> 35
<211> 478
<212> DNA
<213> Homo sapiens

<400> 35
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agttatgctt gtagaagcca actcaagatt aatttacata tttaaaaata ttttccttgg 120

aaatttaata cacatccaat atcgattatc ttctttaagt actttgtatc ttattcttcc 180

tgtcaagctt tgcactataa aggtgatgtc atgcttttct gccatgcctc atgcaggtgg 240

cacctccttc ctcaccccca cgtcttttcc aggtgagccg cgatgcgcaa aaggttggga 300

tgcctggcac aggatgccag ctagtcgatg tctttagaat gcccctgctg tctctcccgg 360

ggctaaatcc tattccaccg tgagccttcc ttgaccagca gagaatagaa gcgcctggtg 420

catacaggcc accaaaggta tctgttgaac agacatgcac acggcttctg ccgtgggc 478

<210> 36
<211> 615
<212> DNA
<213> Homo sapiens

<400> 36
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agtcttcccc caaagacacg ctgatgaatt aatttttctg cttgtcattg taattgttat 120

gtgttgtaac taagaaaata cagagggcat taagagaacc tatgaggtaa ctttgacttc 180

acttcagggt cctggaagga ggaagcaaca atcctaagtg aaacttggac aagaagcacc 240

caataggtag acaaagggat tgagggtatg agttgttagt gaacagaggg aaagaagaga 300

gtgactcaca aaagaagaac acaattttgg aggctaatta caagttagaa ataaaataat 360

gagtgagtac agagagattc actcctcatg actcctctct tgtgtcatct ctcctaggac 420

atttgtcatg tcctcaaaca cgatgcttca aaaaatgctg ctgatcttga tctcttttc 480

agtagtaact tgggtgattt ttataatttc tcagaacttc acaaaggtag gagaaaatca 540

cctttgatgc aaatcacaca ggtaagccct cacctgtgcg accagcctca agtcagttcc 600

actctattag tcctg 615

<210> 37
<211> 392
<212> DNA
<213> Homo sapiens

<400> 37
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cttaattcct ctcctgagca gaggatagca acacttcaaa gattatccta atttttttat 120

ttgcaaaagt ttatttgcag aagttgtttt tgcaaaagtt gaagagtaga taatcccaac 180

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aaaaatgctt tgcattaaca aaagtggaga tacttagatt gatttgctcc attagctgga 300

tccattacat atactacttg atatactgtt ccctagtggt ttgtatatgc cactatagtg 360

aaattcaaaa aaaatgttcc aacctatatt tg 392

<210> 38
<211> 715
<212> DNA
<213> Homo sapiens

<400> 38
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gacaggaact taaactaact tcaagggacc aacacctttg aacaaaaagc cacgttatga 120

accaaaaaaa aaaaaaaaaa cccaaaagta aaacgtttga taacagaatg tggtgctggg 180

acatgaggca gacagtagta atttacagtg tcatttatcg gttgccattt acatgtcggt 240

tgagtttcta gtattttaat caaatgttgt ttcaagtcat cagcacatta gtcaatcaag 300

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gccaggcaaa ctctttgttg atttcattgg ggtggatcct aaaatccaat caggccacaa 420

atgatttgga ctgctgctac ttctctcacc ttgcttctta tttccttcct ctttatgttc 480

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attatttcac ttcattcgaa ccttcctcaa atgtcacctt ctccataaag cccacaatgc 660

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<210> 39
<211> 596
<212> DNA
<213> Homo sapiens

<400> 39
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tgtgcctttt tattacttga ggtatatgga gtctctaatt taaggctaaa tataaaataa 180

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gcccagaatc tgagcaggca tcacttcgca ccagtataaa caggagttgg cgtggaccga 300

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tggaaaatga gaaatatcca agtcctcctg gcagccatga atggattctc tgttat 596

<210> 40
<211> 494
<212> DNA
<213> Homo sapiens

<400> 40

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gagcaaatca atctaagtat ctccactttt gttaatgcaa agcatttttc tggaaaagga 180

gttaagagtt ggtttgttaa tcgacttgtg agcactatga atatggaaag ttgggattat 240

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aggataatct ttgaagtgtt gctatcctct gctcaggaga ggaattaagc atattgggta 360

gattctctga ggccagtcag tggtatttac ccctgacagc tatcagaaga aagatgtgaa 420

accttcctcc gttccaaaca ttgtgggatc tttgttgccc cttttgaacc aatattattc 480

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<210> 41
<211> 542
<212> DNA
<213> Homo sapiens

<400> 41
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caggtatcta aattgcccag ggctccatat gagtggctgc tctgctaata ttccatgtag 120

ctctgcatgt cagactgtag actgggctct ccagtcaccc tagccagtgt tttctgggtt 180

gcagtggttc ccagcctccc tgggatggag gtccctgtgg gagggatggg ccaccatctt 240

tgctgttaca cagccttagc cattgttgcc tttgagctct agggattctg aggtgactag 300

ggactggaaa agtcccccag aacagtgcag ctgctctatg gataaacagc cagactgcat 360

tttcacatgg gtccgaggtc ctagttctct tccccaggca gaatttcctg accacagtct 420

atgaccaccc ccaccagtgt tttctggtca gcagcagttt ccaacctccc tgggatgggg 480

ctaccagagg gagaggtagg ccaccatctt tgctgtttct caacttaagc atggtggcct 540

tt 542

<210> 42
<211> 708
<212> DNA
<213> Homo sapiens

<400> 42
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aatggcatcc gggctgggca cggtggctca cgcctgtaat ctcagcac 708

<210> 43
<211> 592
<212> DNA
<213> Homo sapiens

<400> 43
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gatggagagc gtgcagtgcc gcctcatggg gttcctggcc atgctgtcca ccgaagtctc 120

tgttctgcta ctgacctact tgactttgga gaagttcctg gtcattgtct tccccttcag 180

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ttctcttgga attttcctag gtaaattata ttttttcatt tcctggaaaa acataatttt 420

gctagaaata cgttaaattt cagcaaaggt ggatttgttt gtttcagaaa gtgagataac 480

atagtcaaga ctgtgtcctt tttcacacaa aaaagttttt actattgtgt ttattgaagt 540

tttattaaac tttttattag acaatattta gtgtggaaaa taaagacata ct 592

<210> 44
<211> 459
<212> DNA
<213> Homo sapiens

<400> 44
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aagaattttt caaaattaat tcatttcctt aatacatcca ttatttattt acttttattt 120

atgttttcag tttcctttaa ttgatagaaa atttacatgc agtaaaatgc acagaacttc 180

agtatacaat tcaattattt tggataaata tgtacaccta ggcaattgac atctcaatca 240

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ctcctatcac caaccatgtt tctggtttct attgccatat attagtttat cttgtccttg 360

aatttcacgt aaatggaatc atacactgtg ttctcttctg tgccttcttg aactcaatgt 420

aacattttga gatgcatttt atattacagg atgtaccta 459

<210> 45
<211> 616
<212> DNA

<213> Homo sapiens

<400> 45
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actattcagg taactatttg aatacatttg cctctgtgcc aaggaaaaat aattacttcc 120

aaaataaaaa ggtagcaaaa cctcctccta atcctactaa gataatcagg attcccagaa 180

tgggattgat tataagcctc catacaaact cagcattgtc ttttatttt aaatcagtta 240

gagaaaatgc agctagctgt ctgacatttt ttgtgtgttt ataaacaaaa aaactcacat 300

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ttaatttcct tagccaagag gatacctcat gtatattatg agatttgtca atttatgagc 420

agatgtaatt ttattttctg tgatctttca aaaattttct atgctggata aactacaaat 480

aaacacaaac tttcttgaaa ggaaaatatc taggatttgt aaatattaat tttgaaaatg 540

ttttcttttt aatattgctg attcttacac ttcatccaaa gtacttatta tatttttag 600

gagatataca agttag 616

<210> 46
<211> 525
<212> DNA
<213> Homo sapiens

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taatttacc tacttagggt ctctctctat ttttcctttc agttcatgtt aatttctaaa 120

ttgccatgta taagtaaggg gttgtcaatt tacaccataa aacccttta tgtatccaag 180

gttttcatag gaaatttagg actgtatgat cctaaattgt gctggagtac cacattttct 240

gttaagtagt acttggcaat aaagtatagg aaaaaaaaat cagtgggttg acaaagagag 300

gtcatgatag tgtacctgta atgtaatttg ataaaaaatg tgagcctgaa ctgattgcaa 360

agcattgtta catatagggg aagacattat gggggcagag gggggtgaag atacaaagtt 420

gaataaaact tctctagagc ttcacaatct aataagatag gcatttataa atatctctta 480

aggcgcactt tgttaagtgc taaaatagtg gcacaaagag ctata 525

<210> 47
<211> 526
<212> DNA
<213> Homo sapiens

<400> 47
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ttacacagga agtacagctc ctgaggcaat agaattctta tgtagaaatg tatacttatt 180

acctaatcga gagtgtttgg gtttgcagtt tactaaagtg tacaacagcc aatggctttt 240

atatgttatg tgcaacttgt ttagcccata aactatacta aagtgcataa taagacattc 300

aactacatac ggttactcat tcaagtctgt tatcgattga actgtacata aaatgacatt 360

tgcaggatag tgtatccttt tatttattgt aaggtttctt tgtttatgta tcagcacaca 420

aaatttagta attagcaata ggtctcagtt catttaatgt gaatgagcaa gatctcagct 480

cttactacat tcaattatgg tgtaatagct ctcttgacct ccacct 526

<210> 48
<211> 575
<212> DNA
<213> Homo sapiens

<400> 48
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gccaaaggca aagccagatt tctgaccaat tttgaaatgc ctgaacaggg aagggcatag 540

tggcttcatg tctataatcc cagcatttta agaga 575

<210> 49
<211> 678
<212> DNA
<213> Homo sapiens

<400> 49
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gttagtcacg gtttagtgtt ctttactgca atgctatttt aagatgcaat taaaacgtct 120

cattgccaaa gtgcgtgctt cctcctgggg gcctccttcc taacacgaag gagtcagaaa 180

ccaaggccgg gaggagacct gagctgaaga ctcacttctg gagtgggcac actttgtccc 240

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tgaaccgctt aactcaca 678

<210> 50
<211> 592
<212> DNA
<213> Homo sapiens

<400> 50
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gtattcagcc ttccgtcttt ttttttttta ataccttgct gaattcagtt tgaggctttt 120

aaaaatttta tatttttaca tctctattta tgaatgctgt tagccacctt aggttacttt 180

ttatccccca tccttatctg atttggatgt taaagttata ttagcatcat aaaaagggag 240

tccgatgttg gacattctta ttctgttgta tgcaacctga attattcaga gatttctagg 300

gttttatctc tccctagtat gctgcaggtt cactgttgtg gatcaaacat ggatcatttt 360

tgttcattct gctaaatcag tatttatgat aatcagtatt tatcataaat actgattcag 420

taaatacata aatactgatt cagtgggccc ttgaatctaa agatttgtct ttagctctag 480

aaaacattaa tttcttttga gtatgactgc cccacatttc tttttggttt tctccttggg 540

aaatttgtat tagatagatg ttgggaactt tgggacatat gcctgcatgt ct 592

<210> 51
<211> 355
<212> DNA
<213> Homo sapiens

<400> 51
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atcaaaggca gagttttctg tcttgctatg caacacaatc acctgaatat ctgatatagt 240

aaacactcct gggtaattcc aatatgctgc caaggttgag aacgactcaa actttcagca 300

cctctgggta ttactattac atactatagc acacagttag gtgtgttata tcaaa 355

<210> 52
<211> 637
<212> DNA
<213> Homo sapiens

<400> 52
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tgcacgggat ggtctacaca tctctgattg caataacaca accagtctga taatattctg 180

tacatggact catagcatat tttatggctt acaaaataat agtcaaatgc taataaataa 240

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tattttcctt tcataagtca agacaatggg gaattttaat tctgtaaaga ctcaacatcc 420

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<210> 53
<211> 680
<212> DNA
<213> Homo sapiens

<400> 53
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ttttaaacct cacaaaagct tgacaaatcg tattttctca aaggtcagtt ataatgttga 180

atctgtaact gtactgatga ccttcttcgt actctgttat attaaaatct cttgatctgt 240

gttacacttg gatagaaatt ttttcgcatc attttgtact agcttgcatg agttatttgg 300

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tatcaaaatt gcatttgtca atatcatcat caccttagcc tctaaggatt gggatgctaa 420

taagcttaca gtataagatg caacttttt ccccaaactt gagttttgtc attggcaaca 480

cattctgcca gttattttcc ttgaagtgac aggctaactt tgttattttc ttaagagaat 540

gtgtgccaaa tatccaagtc tgagtaacca tagttcgtct gtcagtggtt ttttaagtgg 600

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<210> 54
<211> 583
<212> DNA
<213> Homo sapiens

<400> 54
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actctatgaa gccaagaaat atgtgtgatt ttgttcacca ttatatctca agcacttggc 180

atagtatctg gcatgaaata gatgcttaat gaactatttg tttaatggat gttgatcatt 240

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cctatggctt gtggctgtga tgatgcatgg cagcactggg gtgcttccga ctggtctgct 360

aaagactatt aataattttt ctatatctgc caataggaat cttatttatt tttgtctgtg 420

gctgtgtttc ctgttcttca gggcacagtg aagccccatt tgcctcaagt tgtttttcta 480

atgattttcc tttgcccata tcctgaacca atttctggtg tatcaaattt ccacagaaga 540

ctgtactcaa gatggcagac caaagcacac atgctgatct aca 583

<210> 55
<211> 634
<212> DNA
<213> Homo sapiens

<400> 55
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tttacggtcc ttgatacatc ttttcaccat tttcaactga aatatatatg taaacatagg 180

gggtagggac cacaatcaac tgcagagaat cttcatgtaa tcataagatc gactgagtta 240

aataaaaaaa atcaaattct gtgagcaaca cataatatat gttcaggatt agaataaaac 300

tatctgcatg aaaaatgttt agaagaacct ctattcatcc acaaatatct tctccttgtc 360

cacaaaccag ggtttgtgca agcctggaaa ttaaatggca taccctttcc tgagtgctac 420

tattcctgag tgctactagg ccagggattt ggcctaggta ctgttgctcg cagcacagaa 480

agccaatcac tgagacaaag agtagtgcca aggaagaagg ctttaatttg gtgctgaagt 540

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tatacagcag ggggaaaata taagtatgtg tgag 634

<210> 56
<211> 431
<212> DNA
<213> Homo sapiens

<400> 56
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tgctgataac accagaagac ccctacattc tctactcaat aggagagcta atgaggtggc 180

atgtgatgta gatccatagt atgtaagaac acaggacaca cacacacaca cacacacaca 240

cacacggctt attaataatg taatgttaaa taatacaatg cagggcattt acattgaatg 300

acggttttgt ttacagcaga tttgctggtt cagaagggac cagttgatcc acttaaacta 360

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caggagctac c 431

<210> 57
<211> 651
<212> DNA
<213> Homo sapiens

<400> 57

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attgagaatt gttgatgtag gttatctggg cagccaccca acaccataca ccaccacctg 180

aatgcagtgc tgccattgca tttatattta tactcatatt tgtaacaaat aatctagtaa 240

cacaatgata tttaactttt catgtttcag taagtataac tggctatcat taagctgctc 300

tgttctatta tcagaacgac agatttacaa aggcagcctt ttattcatgt tgagttattt 360

ttccagttgt aaaatcacct cccacccttt tattgtgcta gtcattcaaa actagaaaat 420

atttttggag gaataacact ggagtttaac aaatgacttt ttaaaaatta gacttgcaat 480

agcaaaaaca acataaagta aatattatgc attttaaatg tttctggcaa ctaagaaagg 540

aacagagaca gacatgaaat gaaaacgacg aaattgtggc aggtgaagtt ccaatgacct 600

tggaaaatgt taccagtaat acttcacaat atataccaag tgatgggaaa a 651

<210> 58
<211> 533
<212> DNA
<213> Homo sapiens

<400> 58
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tttcatcaac ttctccataa tgccatacat gcatacaaat cacactttca gttattcact 180

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attggccaaa tgctgagtat ttttggcttg agatgataac tttattttaa gcctgagaga 300

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<210> 59
<211> 680
<212> DNA
<213> Homo sapiens

<400> 59
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ccaaatgaaa tggtctaatg cacaaacata ttgttttcaa gaaataccag aacttttctc 180

tgactgacta aaggttatta aaaatgtttg ttctaaaatc atttctaatt tttgatttaa 240

gatgtctggt ctctcccttc ccttctttga taaataaggc tgctacattt cctaattttt 300

ctagatgttt acgcaatata ataatgataa aatctaaata atggacgaca aaaaattaat 360

gttacaaaag gaaaatattc attctttttt gtatattttt atgatgatta gggtttctaa 420

tacaaaggaa agcattcttt tgtatttgaa accctatcat tgtgcttgct gaattgaaca 480

ttgctgataa caccagaaga cccctacatt ctctactcaa taggagagct aatgaggtgg 540

catgtgatgt agatccatag tatgtaagaa cacagacaca cacacacaca cacacacaca 600

cacacgggtt attaataatg taatgttaaa taatacaatg cagggcattt acattgaatg 660

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<210> 60
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<212> DNA
<213> Homo sapiens

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cgatgtagag ttgccgtagt ccttcaattt gtaaaatatg caatgtctat gaagcacaat 180

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gaaacaaagt aaaatctgtt ttatttctta taaagctttc ccagagtatc tagtataatt 360

ctgtgcatgt agaagacttc tcagtaatta tccactactc aagagacaac ctgctgtgtg 420

gagtgactga atcctagtga gcctgcccca cagtggccgc a 461

<210> 61
<211> 659
<212> DNA
<213> Homo sapiens

<400> 61
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ttgatactta aaaatagtac agtatgcaga ttactggaat agtgaaaatt gataacgcaa 180

tccctagtag aaagaaaatc cgaaagagtt ctgtataccg gctttcagta catttaaata 240

tatatatgtt tgaacaattc atctttatcc ctaatacaat aacttttcaa aagctaattt 300

ataaatgtca gtttgtacag atacaaactg tataatatcc aatataatca gatattctca 360

gaatatacag attaaatata cagaaataaa tgtatggtta ttgcctgatc ataattcctt 420

agggaaggca ataattcaca atttatgtac ccacagtggc agtgtagaga ggtggttttg 480

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ctaagagatc tccttcctgg aaattatcaa gtatgcatcg aggctacaca atagaaagaa 600

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<210> 62
<211> 649
<212> DNA
<213> Homo sapiens

<400> 62
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agtaagttgc aaaaataatt gctttctatt atgtagctat acagagatga gacagttcct 180

acttccttaa ttcttaaagg agcagaagag tatggcacca ggaatagaac ttggggcaca 240

gcaggttcct ttctactgca gaaaaaggcc attctgaagc cacttatagt tacttctgtc 300

tcccagagcc ttttctgtgc atatgaggtc aaggtcagtg tccatggagc ctggaaggct 360

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caggcatcca aaatgctcag gtgcacatca cagaagggaa aaggaaagaa aatctcggtc 540

atgctccttg gagtttcctc agagaacaag aatttacagc acagctgaat tagggcagag 600

aaaaagacca ccgagtgctt gtccctttt gtgggctcgg gggaaatgc 649

<210> 63
<211> 653
<212> DNA
<213> Homo sapiens

<400> 63
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tcatagtgaa acaacctgat aaataacttc tcaagccagc tgaccaaggt taacattaac 180

agtgattagt tatattgact gcatgcactt ttataggagg cgatataaac agcacttcct 240

catctctact gtcttcctcc caaaaaacct taccccaggc taatcatgag aaaaccatga 300

gacaaaaata ccaactaaaa gccattctat aaaatacttg tccagtaatc ctcaaaaatg 360

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agggaaaacc tggggaatta caaataaact atggacttaa gttgacaata atgtatcaag 540

atcagtttta ttaattgtga tcagtgtacc aggataaagt tttaaaaata gatcagggca 600

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<210> 64
<211> 574
<212> DNA
<213> Homo sapiens

<400> 64

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tttccatata agataacatt tacaggttct ggtaatttgg acatggacat tttttgggtg 540

gagaaaggta ccatttaacc caatacagcc tgtt 574

<210> 65
<211> 558
<212> DNA
<213> Homo sapiens

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aagtttatct acaagtactt atttcattac atttccataa ttattttatt ttaatagttt 120

acctagatta tttacgaaac ctgcaatagt tatcatttaa tgttactttc ctgtcaacca 180

ttttatagct tgtggatttc aggtgtttac cctaagtgag aaccttaagt ttagatacat 240

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taactcttat ttcaaatttt gaccccttat agtattttgg tagagatacg tattgaagtc 420

tcttgactcc agaaaaggga gttttacaga gaaacaaact ttggatgtca actaaattgg 480

ggagattaaa gattctctag agaaagcggg gggctccaaa gcttcagcaa tttgtcctat 540

tgatttgagc cataaaga 558

<210> 66
<211> 277
<212> DNA
<213> Homo sapiens

<400> 66
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gtagagagct gagttctcgc atctgataca ttctattctt gcaatatgtt gttttggttg 240

aaatatgtga caaaaatctg gtctcacaca gacatat 277

<210> 67
<211> 639
<212> DNA
<213> Homo sapiens

<400> 67
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tcaaagcttt gccctgggag tattcttccc ccttgcaaag ctgggtcttg caaagctggg 120

tccttcccat cattcagttc aaaatcacct cctgggatag atcttcccag accaaccaat 180

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ttacacactg atcatctcaa attatcttgt gtattcacta atttgtttct tttctgcacc 300

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acagcaccca tttctctctt gtgaattgct gagactctag tgcccatttc aggactctgt 420

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tatgagatga aaatgaaaag attgccaggt aacactgcag tacagttgaa gttagatagc 540

acgaactctg tattttccaa gactttctcc acctactctt gacagcctgg gtgagaatag 600

aaaggttgac aacagagaca acataaattt tgggcagag 639

<210> 68
<211> 585
<212> DNA
<213> Homo sapiens

<400> 68
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ctggaacaaa tcacagtgga gtctgagatg ggagtgaaaa ctaaatgata tctgcagcct 120

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tgtgagtact ctacttttga tctgcatttg gttgaaaaaa atctgtgtat aaatggaccc 540

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<210> 69
<211> 623
<212> DNA
<213> Homo sapiens

<400> 69
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aggggagacc aaaattcagc caaaattaac tccttgctta aaaaagaaaa aaaaaaggag 180

aaaagaaaag gccaaatcaa caacacgttc aaagataaca gaatccagtc tccacactat 240

atcattgttc agaatataat tcaaaattat tcaacatatg aaaaaacaag aaaaatctaa 300

cccatattca agagaaaaca caaccaatgg agaaaaatcc agatttttt tagtagcaaa 360

aatctgtaag caattattgt aagcagctta aggacataaa ggaaaatgtg ctcacaatga 420

ataaacaaat acaaaatgac agctgagaaa tggaaataaa aaaggtccaa tggaaattat 480

ggaactgaaa atgacattat tggaaataaa atatacactt tccagttatt taaatcttct 540

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<210> 70
<211> 671
<212> DNA
<213> Homo sapiens

<400> 70
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ggttaccatg gaggttacat gtgacagtac aaagttataa caatctattt tgaattaata 180

ccaacttgac ttcaattgca cccaacactt tgctttttta caactttccc ttcctgcttt 240

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ttataattat ttttgtgaat ttgcctttta aattctttaa aaaataaagt gtagttacaa 360

gccaaaatta tataaaacta ttagttttta taatgtccat gtatttgcct ttaccggaga 420

tctttatatt ttcctatgtg ttcaagttac tgtctattgt cattttattt caactttgaa 480

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<210> 71
<211> 636
<212> DNA
<213> Homo sapiens

<400> 71
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aaataatttt ccaggaatat ccccaaagtt tttgggctgg tatatcatat aatttctttc 180

agtaattgtg tggaaaaata ctttataaat gcatagatat agatagatat tttcatataa 240

tacatgcagt gatgatctga tgagaaaaat gatgtaccct gaatgtttta tcttttaata 300

gcactggcaa tcttgatatg catgaatctt ttaaaaccat gctacaaacc tctgtttcat 360

ttagaatatt atgtcttttt tgacttaccc caaaccccaa aatgaccaaa tgggaatgaa 420

atatgccagc atgcacctca tgcctgggaa gatacataaa acaatgggtt gaggattgga 480

ttaaagaaag acaaaaggcc ttcacacaag tgattcttcc taaaattgaa aggttaccag 540

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aacaattata tgtgtgtgta gtgtgtgtgt gtgtgt 636

<210> 72
<211> 658
<212> DNA
<213> Homo sapiens

<400> 72
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<210> 73
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<212> DNA
<213> Homo sapiens

<400> 73
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<210> 74
<211> 660
<212> DNA
<213> Homo sapiens

<400> 74
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<211> 487
<212> DNA
<213> Homo sapiens

<400> 76
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<211> 531
<212> DNA
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<212> DNA
<213> Homo sapiens

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cagtgagtta aacctctgtt ataattcag 629

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<400> 83
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<212> DNA
<213> Homo sapiens

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<212> DNA
<213> Homo sapiens

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<213> Homo sapiens

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<212> DNA
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<213> Homo sapiens

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gagccagata tgctgattct ctaccatttt caaaagagga attggaaaag ggagagcttg 360

tttatgtggt attcacaata gtgtctgctc ctgaagaaaa tttttggaaa aatctcatga 420

gtgtcctcag actgaaaaca gggatccagt ctgttgttca tgcaggactc aggaggcgag 480

cgagcatgtg ataccaggaa gggtcccatc cctgccctgc tggggagccc tcagtggcga 540

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gcaggcagag acactatgca tacagatacc ataataatag taaagaatgg ttgagtggag 180

aaccagtgcc tctgttccaa ttatttttat aattgctctc tatctactat ctctacagat 240

attccataaa cagtgtgcaa cactaactcc atcctttcgt tgcatttgtt attatttttg 300

ctatagacaa aattttcaac catgcagaaa caaaagttta aaaccgttac attgttctct 360

gcatttacag gtttgcagta atgtagggta attagacatg ctgttaaatg accaaattaa 420

acacatcatg ttttggtaaa gaaacgaacc caagaagtag taaagatggt ggggaattcc 480

tgaatcccaa aagccttctt aattttgacc attggacatt catatatgtg tgtgtgtgta 540

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<212> DNA
<213> Homo sapiens

<400> 99
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cagacaaagt tatgggatac ttagtcacca caaaactctg gcttgaaact tgtctccttc 480

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<212> DNA
<213> Homo sapiens

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ttaaatgcca tttgttgaaa gccaataaat acatatatat gtctagtgca caactcacag 240

aagatatcct taatctactt atactggaaa catacttaca acaaaggatt ttgatggaca 300

tagcgtgagt tgtattttca gctttaatga aagatctcat gccaatgaca aaaagatttc 360

caaagcaggt aatgaaagct ataacccaga caaatattct gaggatattg ttagccaaga 420

ggtcctcaaa tgaagaaatg ccgtccgtca agggcataca tattcggaca tggggagcat 480

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gcagcaatga tacagaacct acagttgcag tcctat 576

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<211> 657
<212> DNA
<213> Homo sapiens

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tggctgtgtg ctctgtgctc acccacctgt gaatcaccgg gtggtacaga gtgacaatcc 180

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tatttggagg tatctgtatg acaactctaa cccgaaattt catatttggc acagccatgg 300

cctgtgggga tggctggcat tctggatatg ttggaaacag cactggttag acatggagca 360

atgtccaagt gccagcccca ctcatctgct acacgtgctg tgctattctg cttcactcgc 420

acaaaactag actgcagcgc aatataccgg ctcatccttg tgtggttctc cagcactcac 480

gggcaattat ttctccattt ctatgtgttt taaacctgtt ttctctccga cctgtcaatg 540

agagcatgaa cctttatgaa ccccacctcc ctggaccctc ttgataggtt tcgtggaagt 600

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<211> 547
<212> DNA
<213> Homo sapiens

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ccacatccag tatactacag aaagagtgtt tcaaacctgc tctatgaaag ggaatcttca 180

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tgaggacaca tatcaccaac aagtttctga gaatgcttct gtctattttt tatgggaaga 420

tatttccttt ttcaccgtag gcgtcaaggc gatcgaaatg tccacttcca caaactacaa 480

aaagagtgtt tcaaacctgc tctatgaaag gccatgttca tctctatgag ttgaatggaa 540

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<211> 762
<212> DNA
<213> Homo sapiens

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gcaatattac aaatatataa atgatgaccc aaatatgata cataaaaaat gcctttgtga 120

tctcaaacac acagaggtag gtggaactaa gcctgtggac tctaggatcc aggctctgaa 180

tctgtcattt agcagaagta gcctggagtt caattcttca aataactgga agctgtgatg 240

tctctggagt gacctgtcct gcatcaagct gtgtcttgga ggtagcacag ggacctgaga 300

caacatagag tgaactgctg gctcaagccc cctgttacac tgggtctgca atactgccaa 360

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atgcagttaa gaataagcag acgtgagaac aggtggagaa acactctctc tctctctctc 480

tcttgccctc tccctctctc ctactgaaga tgagtctgta tattaaaatt ctaaagcaca 540

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agcacttcaa ataatagagc aaagcctgaa ctgaacttaa atgaagtata tttgattcct 660

cagagataaa ggtggtaata acacctataa agcaagcata agaaatcatg agccaaaaaa 720

caagagtcaa aaaggcttgg gaagtttggg tgtggtggca ga 762

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<211> 515
<212> DNA
<213> Homo sapiens

<400> 104
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aaaatgctcc cagatgtttg atgcatgaga gggaaaatgc caggaacaag gatcaaattg 120

aggtgggttt cagacattat aaaatctgtt gatgtaaaaa ctaagaaaac aaataagatc 180

ataggcatga aatccttctg gaaggtcaat aatgataaag ttttactata ttaaaccgat 240

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ttgctaatcc ataataaatg gtacattaac tatgatccaa cttatctttt ctacacaagg 360

gccacgggac tgcatgtgga taaaatctgg actggattta ttttttagg ggcctgatcc 420

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aatcatcata attatagtat ccctctgact tcaaa 515

<210> 105
<211> 344
<212> DNA
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ttttttaaat gacatttatt tctgggtttt cacacatgtg ctttacatgt tcttgttttc 180

ctttacaatt gaacatacac tctatcagcc agaggccagt gagcatttga tgggggccaa 240

aaataaaaaa aaaacgagtt ttggcatagc taatactttt catctttgcc tcatccatat 300

taagtttgag tcttgggctt attattaatt tgagcacttt catt 344

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<211> 453
<212> DNA
<213> Homo sapiens

<400> 106
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tggataagaa agttcacagt aagctttatt caaaagaccc caaaactgat aacaacccaa 180

atgttcacca cccagagaat gaataaacaa atcattctgc attcttaaac aaaacaaaaa 240

caaaacaaaa ccactccatg gcaaacaaaa ggagaaaatg cctgatacac acaacagcat 300

gggtgaatat caagaacatt tgctgagtga aggtacagtt atacagtagc gcattctgta 360

tgggtccaca tacacagagt tctagaatat ataaaaaaaa aactattcta aaaaaggaaa 420

taaaaacagt tgtattgttt ggggaggtgg gga 453

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<211> 335
<212> DNA
<213> Homo sapiens

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actcacacag cagctggccc ccaggttacc cgcccttcat gtacatggcg atggtcacct 180

ggctcaccag caaagtgaac aacaggtcgg tggcagccag ccgcataact gtgtagaagg 240

tggtctcctt ctgctccttg cgcgacttgc acagcaccac gatggccacc aggttgccca 300

ccaccccgaa aatggacggg tcccaagctg tccag 335

<210> 108
<211> 573
<212> DNA
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tttcagaaga aaattgctaa atatgccaag gtgtcatatt attttttttcc cagcatatta 180

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gggatttgcc agcatcttat aattttgtac aataaatgaa gcacccatgc agtgcacaca 480

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ttgagacaga gtctcgctct gtcacccagg ctg 573

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<211> 663
<212> DNA
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aaaaaaaaac ttctggtggc ccagaagggt tgagttgatc aaagtttgaa ctacacactg 240

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gctcggaaaa cactgtaaaa gctgcctctt taataaggat cctggtgtcc cgtgatggat 600

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<211> 590
<212> DNA
<213> Homo sapiens

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taatcacatg aggaggaaga taatgggaca aacaactggc ttcaggattt ttttttcttt 180

tctgagattc acaccaaatt tctgcatgct tgagatttac tttacctaaa atttttaggc 240

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<211> 651
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<213> Homo sapiens

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tcaggcagcc cgcatgagag atgactctgc tatgcaactg catgtccaca gtcatcttgg 180

gaaccgtggc cgaggtgaaa ctgaggttag cccagcacag gttggagagg aagaagtaca 240

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ccgtgaccag atacatggac agggacaggg acagcaaagc aaggaccggc tgcagttctg 360

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cttcatgctg aatgcaagca attcacaagg gaacattttc acacttgcag accatacacc 540

gccagcaatg tttctcagtt gtgacaaatc caaaaatctc agaattgtta catgttttac 600

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<210> 112
<211> 623
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<213> Homo sapiens

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<210> 114
<211> 707
<212> DNA
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<211> 681
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<211> 678
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gttcatgatc aaggtgtcgg caggtttggt ttcttctgag gcctctctcc ttggctcaca 240

gaaggacgtc ttcttgctgt gtcttcacat ggctgtccct ctgtgtgtgt ttgtgtccta 300

atctcctctt cttataagga cacctgttat gctccatcag ggcccatctt aatgactcca 360

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aatgttatgt ttaacataac aagtttaaca aaacttgcaa aaacatcttt cagatacttt 540

catattaaaa ttttccttgt gcagtgattg atcctaagta ctctgaacta ttgacatttt 600

aactaatttg atggctaggt cctcattata ttagtttatt gccatctctt tgtagacatc 660

aaagcagcaa aaaaggaa 678

<210> 117
<211> 697
<212> DNA
<213> Homo sapiens

<400> 117
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tctttgagtc agtggttgaa tgcctctcac accagagggt gaggtcttgg aagggaggaa 120

ctgcagttgg taggctctgg gtcaaggaga cctggattca agtcctgcct ctctaactta 180

ctggctttgg gcaaattact taacctggct gagccttggt ttcctcatct gtgaaatgca 240

gttgctgtga ggatttgatg agccaatgca catgagactt gaggagtact ggctgtgaat 300

gcaagggttg cccttggtgc tctctcttca tccctggagc ctggccctgt gcagggctgg 360

gaggatgcag gtgcttggaa gatgggcttg gctaatggga gtcgctgtgg cttttgcaga 420

tgaatatgaa tgccaggcct gcccgaataa cgagtggtcc taccagagtg agacctcctg 480

cttcaagcgg cagctggtct tcctggaatg gcatgaggca cccaccatcg ctgtggccct 540

gctggccgcc ctgggcttcc tcagcaccct ggccatcctg gtgatattct ggaggcactt 600

ccagacaccc atagttcgct cggctggggg ccccatgtgc ttcctgatgc tgacactgct 660

gctggtggca tacatggtgg tcccggtgta cgtgggg 697

<210> 118
<211> 673
<212> DNA
<213> Homo sapiens

<400> 118
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tattaaatat acataaaatg tatgtaaaat ataaaaatat ataaaatata tgtaaaatat 120

aaaatatatg taatatttat actataaaaa tatatataaa tgcaggggtt taaaatcata 180

tttatatgat atatatgtaa aatcatatat gtgtgtgtgt gtatatatac atatatgatt 240

ttaaaaccct gcatttttta tattattgga gtagaaccaa tccttttgtt gataactaaa 300

agctagccac ggatacattt gcctagattt tttgatttat ttgtgagctg ccaaggatgg 360

caacaacttc aagactttct ttggcaataa aacatagtca acatatttaa ataaacaaac 420

atttaaataa atataccgta aagtataatt aaacattctt taaaatgaaa acacttgatt 480

aaaattattc ctaaatggag tatcaagatt ttgatactta taagagatta tggtgtctgt 540

gaaagaattg ataaatagat caatagaagt caagaaagtg gttacttttg gagaagggat 600

acagtgggga ttttgattgc taccaatgtc caatttcttg accctgtgtg atagtaaatc 660

atttgactct aca 673

<210> 119
<211> 495
<212> DNA
<213> Homo sapiens

<400> 119
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ccaaaaacag tggtaaatac tgaagatata aagatgagta agttcttgta ctcaagaagc 180

ttatggtcta gtaaaaaaaa aaatgcagtc atgcaaacaa ataaagacaa aaggatatca 240

aatgtgaaac aatacataca gagctttaca cagaaatatg tagtcattac aaggagagtt 300

ggaaaatgct ttaaaacaag gtaatagctg atctgagttt tgaaagctga gcacgtcttt 360

agcaagaaag caagcataat agatgactca aaagccaaaa tgttactatc cgagtgacat 420

ggattgctgt tataagatag gtagaatcta aaaattgtgt ttatgtgtgt ctaaaatatg 480

tctctgcgtt gcact 495

<210> 120
<211> 675
<212> DNA
<213> Homo sapiens

<400> 120
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agaacagctc gcaaaactaa gatatgggac ccaagaatgt agaggaaggt gatgaagatg 180

atgagagagc ttactgtagc acaagtcaga gtagttttgg gaactggggc acaggacagt 240

gccagcaatg gtcccaggtt acagaaaaaa tggtcagtga tgttagggcc acagaaaggc 300

actcgggaca taagcactgc aggcatcagt atggatagaa aaccacctgc cctgcagaag 360

gccactaatc ggacacacag gtggtgagtc atgactgtgg gataatgcaa aggtcgacag 420

atggtaagga accgatcaaa ggacatcaca gacagaaagt agccttctgc agcacacatg 480

gagaagtaga agaactggag caggcagcca gcataggaga tgctcttgat atgggagatg 540

agattggcca acattttggg acatcagaac taatgcagca gatctccagg aaagagaaat 600

tagccaagag gatgtacata ggtgtgtgga gtttctggct tgaccacaca gcgcagatga 660

tggatgtgtt accca 675

<210> 121
<211> 572
<212> DNA
<213> Homo sapiens

<400> 121
gtgtgacctt gggcgtgtca catgacttcc tgaactgtgc tgttgtctgt aaagggaggt 60

ggtcagactg ggatcctctc caggattgca ggcctgtctt attatcttgt tttacttcag 120

tctgccagga tttctttctg gaactccctg tggtcccagt tgccggattt cagagattgc 180

tgtggggaat gccatggaat agaatctggc caccttgagc tgagaaaggt gtttgtgatt 240

gatggttgat gccaccaagc aaacagggtt aagcaacttg actgcctgcc tgctgctttt 300

aaaaaggcag ctgacgacct aattctgttt agaattaggg gcgaagctaa ggaaactggc 360

tcaggctgtg agtatcatct ctagattcag atttctggga ccacatcaga aaccaggttt 420

tatgtggacc tttgatgggc agtgtggtgt gcaacgtggg ggactgtggg ttttagactg 480

ggcagttctg gctggggatt ccagttctac cccttagcag cattgttggg aggacgaaag 540

ggaaatgccg gatgggaagt gcaagatgca gc 572

<210> 122
<211> 600
<212> DNA
<213> Homo sapiens

<400> 122
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tcgttattca gatgataaaa gcctcttcct tctctatttt tccatttgca ccatcacacc 120

aggggaaatt atggagatga gaaatactac cccagacttt attctcctgg gactctttaa 180

ccacaccaga gcccaccaag tcctcttcat gatggttctg agtatcgttt tgacctccct 240

gtttggcaat tccctcatga ttctcctgat tcaccgggac cggccggctc cacacgccca 300

tgtacttcct cctgagccaa ctctccctca tggacgtgat gctggtttcc accactgtgc 360

ccaaaatggc ggctgactac ttgaccggaa ataaggccat ctcccgcgct ggctgtggtg 420

tgcagatctt cttcctgctc accctgggtg gtggagagtg cttcctctta gcagccatgg 480

cctatgaccg ctatgcggct gtctgccacc cactccgata tcccactctc atgagctggc 540

agctgtgcct gaggatgacc atgtcgtcct ggctcctggg tgcagctgac gggctcctgc 600

<210> 123
<211> 662
<212> DNA
<213> Homo sapiens

<400> 123
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ctcagttttt gtatttgcaa aatggcagtg ggtcagaccc cttagcctca aagggccctc 120

ccaacctctg gcacttgagc atctctgagc ctgctgggcc acctgtccca gtgcctcttg 180

ggctttggaa gttgaatgct gcaaccccaa gccccagttt caggtaggga tgagcccatt 240

gcccaatgct ggggtccgag tgggcctgaa ggctcccaga ggaccacgtt ctcagccctg 300

gatgggcagg gaccctggag acctggcctg tgtggacaca ggggagtaag tactgggact 360

gagcctgtag ttttgcttct tccacccaac ccgttggggg tcgttctcac agcttggtgc 420

tgggtacacc aggggactca ccattggagg gatccgatgg gttccaaggt gcacaaaaca 480

gacccccagg tcatcctcag gtggtctaca cagcctgtgg ctaaagcaac tgctgtctcc 540

agcacttctt agcttcagtc tggtgaaagg aagaaagtcc ccttggcagt gtcttacagg 600

cagtcataga gggaccccac agcctggcca aaatgctcaa tttcagaaaa tcccagactc 660

at 662

<210> 124
<211> 660
<212> DNA
<213> Homo sapiens

<400> 124
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agctttccaa tagggaaaac attcagtcta gtagcttgtt ctgctactag actgcctcag 120

tgaatgagta actgactgga ttaaacaaaa caccccagaa atatttacca agaaggtaag 180

gtccaaaagg aaggtagtga aaggaaatgt actctgatca tgaaatggtt ggttgatgag 240

caagtcaagc ttgaagattt atctcttttc ttcattcaga aaagcaactg aaatgcaaac 300

tggtgctatt aataacatag tccttgaaga caacctaaaa atagttccta aaatgccatt 360

tgtaactgta attttgcatc tcaatcattg gcagtttgga atgacagtat tttgtacagc 420

aagatgatgc acattataat actatatata gagagagaga catgcatgtg ctcctccttc 480

ttccccacac aaatcacccg gaggtcataa aaatgtttaa gttccaccag gagtaagcaa 540

aaatttaaca aggaaataca tactcatttt acatttaggt aattaagtag taatctcctt 600

gatgttaatt tttatttctc caagttaaag ttcttgctta tatgaactct tgctttctaa 660

<210> 125
<211> 680
<212> DNA
<213> Homo sapiens

<400> 125
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agagttacag acataattat aaatcaggta ggttagggag atacaagttt catttaagaa 180

atgaactgta ggggaaggta gtggggaaga gggatcagga gaggttggcc aatgggtaca 240

aagttacagt taggaagaat aagttctggt gttttgttgt acagtagggt gcctctggca 300

aacaacaatg tagtgtatac ttttaagata gctagaagag aagattttga atgttatcac 360

cactaagaaa tgatcaatgt ttaaagtagt aaatacagta atgaccatga tttgatcatc 420

atgcaatgta tacactcatt gaaacatcac actgtacccc ataaatgtgt acaatcatta 480

tgtcaattat aaatattaaa aattaatttt aagaagaaac gcagaaaaaa atgttaacag 540

tgttctaaag gaagggacag ttgcatcgga aagacttgga aatgtgtaag gtgacagtca 600

agagaaatgg gagtttatgg tgaccgagta ggatatggat caaggtaacc accagcaatg 660

ggtgtgaagc attgcatatg 680

<210> 126
<211> 642
<212> DNA
<213> Homo sapiens

<400> 126
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ctgggcttcc gcatgcgcag ggaacgccgt ctccatctac atcctcaacc tggctgcggc 120

agacttcctc ttcctcagcg gccacgttat acgttccgcc tcactcctca tcaatatctg 180

tcatcccatc tccaaaatcc tcattcctgt gatgaccttt ctatacttta caggcctgag 240

ctttctgagt gccatgagca ccgagcgctg cctgtgcgtc ctgtggccca tctggtaccg 300

ctgcctcctc cccccacaca cctgtcagcg gtcgtgtgtg tcttgctttg ggccctgtcc 360

ctactgcgga gcatcctgga gtgaatgttc tgtgacttcc tgtttagtga tgctgattct 420

atttggtgtc aaccatcaga tttcatcaca gtcgtgtggc tgatttttt atgtgtggtt 480

ctctgtgggt ccagcctggt cctgctgatt aggattctct gtggatcctg gaagatgcct 540

ctgaccgggc tgtacgtgac gatcctgctc acagtgctag tcttcctact ccgcagcctg 600

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<210> 127
<211> 558
<212> DNA
<213> Homo sapiens

<400> 127
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tcatcagggt cttctaaagc atagggctca gggaaggagg gttatcaaca tctggccaag 120

ggctggagat ggaaatgttt ccagacccta aagcaagaaa aagatcagca ggttagagaa 180

aaagtaagat ggccacttac ttagagtgaa tttagataag aataaaagcc gtgccccagg 240

agtaggcaag aggctgatta ttgagatcct gtaacccatg ggaaggaacc ctaatcttat 300

gatgctggtg atgagaaagt gttggtgggg tagagtaaga gaacacatta atctgctttg 360

cctcatggaa agaataaatt ctggtagaca tatgtagatg cagagagtga gctattatag 420

tttttgtaag agagattatg gtttgactta tggtgacagt gatggacatg gtgagcaatg 480

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actgagaggt gacaatgg 558

<210> 128
<211> 596
<212> DNA
<213> Homo sapiens

<400> 128
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ggactgaaaa ttatgaggaa gaaacatttg tccttggtgt ttctgaaata tgtgaaccaa 120

accccaatgc ctgcactttt gctctcacaa acttctgaca tgaggcacag atttttacaa 180

aacagcttaa catagaagtc tcacaaaatg tgcagatttc ctcagatccc aaaaacaatg 240

gaaaagcact cagaccacaa gagcttcatg ggaatagcag aaagaagagg cgaactttgg 300

ctgtcactgt gaatgccctg gaatgttagt ggatgaacag agaagcctta gaagatttaa 360

gagcataata agcatagggt aggaaatttc cacctgtggc agcaaaagaa gtaaatttag 420

aattttccag aaccaatttc tttgaagcag aacttccaac accacatttt taaggttttt 480

ctccttggcc tttgcacctc tcatctttgt tatttgttca ttcttcccta ttgggctgtt 540

gcctattatt gtctctcttt ttacattcca aagaacattt cctttactgt aggaca 596

<210> 129
<211> 180
<212> PRT
<213> Homo sapiens

<400> 129

Leu Pro Ile Arg His Tyr Pro Ser Ala Thr Ser Ile Phe Leu Ala Tyr
1 5 10 15

Ser Ala His Phe Leu His Leu Thr Gln Asn Gln Lys Pro Leu Val Pro
20 25 30

Leu Ser Ser Pro Thr Pro Thr Ser Thr Ser Leu Leu Pro Phe Ser Gly
35 40 45

Leu Pro Phe Phe Arg Phe Ile Phe Ser His Ser Leu Trp Asn Leu Leu
50 55 60

Pro Ser Ala Phe Thr Pro Thr Gln Leu Thr Ser Phe Pro Ala His Cys
65 70 75 80

Pro Pro Leu Ala Asn Gln Pro Ala Gln Phe Ser Ser Val Phe Thr Val
85 90 95

Pro Asp Val Ser Ala Ala Ser Ser Cys Ser Leu Pro Pro Ser Trp Lys
100 105 110

His Val Leu Pro Trp Leu Pro Gly His His Ser Val Phe Phe Ser Ser
115 120 125

His Trp Leu Leu Leu Ala Ser Phe Leu Phe Ile Ala Phe His Asp Phe
130 135 140

Asp Ser Pro Trp Thr Ala Gln Gly Ser Val Leu Glu Leu Phe Leu Phe
145 150 155 160

Phe Pro His Ser Val Pro Pro Pro Leu Val Ser Trp Ser Gln Ile Pro
165 170 175

Cys Leu Pro His
180

<210> 130
<211> 186
<212> PRT
<213> Homo sapiens

<400> 130

Leu Asn Ser Glu Cys Tyr Asn Leu Cys Tyr Asn Gln Leu Ser Lys Ser
1 5 10 15

Tyr Val Tyr Thr Tyr Ala Tyr Phe Phe Cys Asp Leu Asn Leu Gly Gly
20 25 30

Gln Pro Tyr Leu Val Ile Phe Val Lys Val Thr Lys Leu Gln Tyr Ala

```
        35                  40                  45

His Phe Ser Lys Cys Ser Arg Leu Leu Ile Met Leu Gly Ser Phe Ile
    50                  55                  60

Ile Tyr Gly Phe Ala Lys Thr Asn Cys Lys Ile Gln Tyr Ala Leu Ser
65                  70                  75                  80

Tyr Ile Ile His Thr Tyr Ile His Ile Tyr Glu Lys Glu Arg Glu Arg
                85                  90                  95

Glu Arg Gln Arg Tyr Leu Asn Trp Asn Gln Val Lys His Ile Ser Thr
            100                 105                 110

Asp Pro Lys Phe Leu Lys Asn Ile Ser Leu Val Phe Phe Lys Pro Leu
        115                 120                 125

Val Asn Ala Thr Thr Asn Gly Tyr Ser Val Leu Phe Leu Gln Phe Ile
    130                 135                 140

Leu Leu Ser Ser Lys Leu Leu Lys Ile Phe Val Cys Leu Cys Ile Phe
145                 150                 155                 160

Ser Leu Glu Thr Ile Leu Gly Ile Leu Asn Lys Gln Pro Leu Ser Gln
                165                 170                 175

Glu Thr Leu Ser Glu Cys Trp Gly Gly Arg
            180                 185
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<210> 131
<211> 144
<212> PRT
<213> Homo sapiens

<400> 131

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Phe Gly Gly Leu Leu His Gly Cys Met Lys His Thr Ser Cys Lys Leu
1               5                   10                  15

Lys Ile Asn Lys Leu Gly Leu Pro Ser Leu Gly Pro Leu Pro Phe Tyr
            20                  25                  30

Gly Ser Ser Val Phe Thr Leu Leu Asn Leu Ala Thr Val Leu Phe Trp
        35                  40                  45

Ser Val Phe Val Met Ala Gly Ala Glu Phe Ser Leu Ala Val His His
    50                  55                  60

Cys Cys Leu Leu Pro Ser Gln Thr Arg Cys Leu Pro Ser Leu Ser Ile
65                  70                  75                  80

Arg Gln Ser Val Arg Cys Ala Pro Asp Pro Ala Ser Cys Pro Leu Pro
                85                  90                  95

Phe Leu Ile Gly Leu Lys Ala Cys His Cys Ser Cys Thr Ala Lys Arg
            100                 105                 110

Pro Gly Ala Ser Ser Ser Ser Ile Leu Val Thr Gly Phe Cys Gly Phe
        115                 120                 125

Ser Ser Val Thr His Gly Phe Ser Ser Asn Thr His His Met Ala Gln
    130                 135                 140
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<210> 132
<211> 183

<212> PRT
<213> Homo sapiens

<400> 132

Leu Gln Ile Asp Tyr Ser Ser Ile Lys Asn Cys Gln Lys His Glu Gly
1 5 10 15

Pro Lys Gly Glu Thr Asp Ile Gly Lys Ala Leu Val Val Val Glu Val
20 25 30

Gln Gly Leu Ser Pro Asp Cys Ser Ala Ser Ser His Ser Ser Leu Pro
35 40 45

Ser Arg Leu Ala Pro Ser Phe Pro Arg Ser Pro Gly Phe Ser Val Thr
50 55 60

Tyr Ser Glu Lys Tyr Cys Pro Ala Glu Leu Asn Ala Ser Ser Ser Thr
65 70 75 80

Tyr Leu Leu Gly Pro Phe Ile Phe Leu Pro Leu Ala Ser Phe His Leu
85 90 95

His His Leu Val Thr Ser Cys Leu Leu Tyr Val Phe Leu Tyr Leu Leu
100 105 110

Pro Ser Tyr Ile Leu Lys Ala Leu Phe Phe Leu Lys Gln Ile Leu Thr
115 120 125

Phe Leu Leu Ile Leu Asn Met Leu Leu Phe Ser Ala Trp Lys Thr Ile
130 135 140

Leu Lys Leu Thr His Pro Gln Lys Leu Phe Lys Asn His Leu Arg Ile
145 150 155 160

Gln Leu Lys Ser Glu Pro Ser Leu Glu Arg Leu Gly Lys Gly Thr Pro
165 170 175

Phe Asn Val Ser Thr Ile Ala
180

<210> 133
<211> 123
<212> PRT
<213> Homo sapiens

<400> 133

Ile Glu Phe Val Leu Ser Arg Thr Pro His Ser Pro Thr Tyr Ile Tyr
1 5 10 15

Ala Pro Pro Met Cys Asn Ala Asn Glu Glu Asp Leu Ser Met Leu Leu
20 25 30

Thr Pro Lys Gly Glu Ile Ser Val Thr Asn Lys Leu Asp Asn Ala Phe
35 40 45

His Gly Asn Thr Leu Glu Phe Ser Ser Glu Phe Tyr Lys Trp Ile Leu
50 55 60

Phe Tyr Glu Val Thr Ser Phe Phe Ser Pro Cys Met Tyr Ala Ile Asp
65 70 75 80

Tyr Ser Lys Asn Val Tyr Ile Phe Leu Phe Ser Ser Phe Lys Ile Ser
85 90 95

```
Val Glu Leu Gln Ser Val Tyr Leu Ile Ser Ser Val Ile Lys Asn Leu
            100                 105                 110

Thr Lys Lys Leu Ile Ser Thr Ile Val Gly Lys
        115                 120

<210>  134
<211>  66
<212>  PRT
<213>  Homo sapiens

<400>  134

Gly Pro His Pro Thr Leu Trp Phe Ser Leu Leu Arg Gly Asn Gly Leu
1               5                   10                  15

Ala Pro Cys Arg Ser Leu Trp Glu Ala Asn Thr Phe Thr Arg Glu Pro
            20                  25                  30

Trp Asn Pro Ala Pro Leu Arg Gly Pro Gly Arg Gln Trp Gly Leu Ala
        35                  40                  45

Gly Leu Pro Val Leu Asn Ser Cys Ala Pro Asp Trp Val Pro Trp Ser
    50                  55                  60

Tyr Ala
65

<210>  135
<211>  132
<212>  PRT
<213>  Homo sapiens

<400>  135

Asn Ser Ile Phe Met Lys Asn Val Leu Thr Leu Val Val Leu Val Arg
1               5                   10                  15

Gly Ile Phe Phe Phe Gln Ala Tyr Ser Phe Pro Asn Asp Tyr Ser Phe
            20                  25                  30

Cys Trp His Phe Ser Glu Gly Ile Leu Glu Ile Ser Leu Arg Val Arg
        35                  40                  45

Lys Ala Thr Asn Cys Arg Gln Leu Pro Val Gly Leu Thr Phe Cys Arg
    50                  55                  60

Ile His Ala Trp Cys Ala Glu Gly Gly Gln Gly Val Lys Asn Arg Lys
65                  70                  75                  80

His Leu Met Cys Glu Phe Ile Ser Gly Ser Arg Arg Leu Pro Leu Arg
                85                  90                  95

Trp Leu Met Leu Pro Ala Val Pro Pro Met Ser Ile Leu Gln Gly Leu
            100                 105                 110

Ser Val Leu Trp Gly Tyr Glu Gln Ala Ser Glu Trp Gln Asp Tyr Leu
        115                 120                 125

Glu Asn Leu Gly
    130

<210>  136
<211>  189
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<212> PRT
<213> Homo sapiens

<400> 136

Ile Leu Val Gln Thr Ala Phe Val His Arg Lys Asn Leu Lys Glu Tyr
1 5 10 15

Asp His Leu Val Val Leu Leu Pro Val Lys Tyr Cys Cys Val Ile Phe
20 25 30

Tyr Ser Ile Tyr Ile Ser Asn Thr Ser Met His Leu Val Ile Leu Cys
35 40 45

Asp His Leu His Asn Asp Leu Phe Asn Thr Gln Gly Lys Cys Ile His
50 55 60

Pro Tyr Val Ser Asp Glu Lys Ile Pro Asn Ser Phe His Cys Ser Glu
65 70 75 80

Ala Phe Glu Thr Gln Ile Ser Cys Leu His Pro Ala Asn Asn Gln Lys
85 90 95

Ile Ala Asn Cys Gln Tyr Cys Lys Asp Gln Thr Pro Lys Cys Pro Thr
100 105 110

Arg Pro Cys Trp Pro Ala Pro Ser Ser Leu Ser Ser Leu Thr His Val
115 120 125

Ser Leu Arg Glu Ala Ala Pro Leu Val Ser Tyr Gln Cys Leu Gln Ser
130 135 140

Leu Ile Cys Leu Leu Ala Thr Gly Ser Leu His Val Leu Ser Tyr Ala
145 150 155 160

Phe Phe Gly Leu Cys Leu Phe Leu Leu Leu Asp Gln Glu Leu Thr Asn
165 170 175

Phe Ser Leu Pro Ala Lys Phe Asn Tyr His Leu Phe Leu
180 185

<210> 137
<211> 200
<212> PRT
<213> Homo sapiens

<400> 137

Leu Asn Ser Leu Arg Ala Cys Ser Asp Ser Leu Ala Tyr Ala Thr Ser
1 5 10 15

Gly Asn Arg Ser Phe Phe Lys Ile Thr Cys Ala Asp Leu Val Thr Gln
20 25 30

Gly Asp His Thr Tyr Tyr Phe Leu Ser Ile Arg Asn Tyr Leu Trp Lys
35 40 45

Gln Asp Asp Phe Ile Ser Cys Leu Ala Leu Pro Leu Leu Phe Thr Glu
50 55 60

Asn Gln Gln His Ala Asn Asp Val Leu Lys Val Gln Ser His Leu Arg
65 70 75 80

Thr Leu Gly Ser Leu Ala Arg Glu Thr Leu Tyr Asp Thr Val Phe Lys
85 90 95

```
Cys Thr Pro Ile Gln Asn Cys Lys Tyr Leu Phe Cys Thr Asp Leu Ala
            100                 105                 110

Cys Thr Lys Gln Pro Tyr Thr Val Tyr Ile Lys Cys Thr Ser Arg Leu
        115                 120                 125

Ser Ile Arg Lys Arg Gly Lys His Pro Asn Tyr Ile Gln Arg His Tyr
    130                 135                 140

Trp Lys Leu Ile Met Tyr Asn Ser Gln Tyr Asn Ala Asn Ile Tyr Pro
145                 150                 155                 160

Arg Val Ile Gln Phe Leu Thr Val Gly Glu Ile Ala Phe Ile Pro Asn
                165                 170                 175

Leu Thr Leu Leu Arg Leu Lys Gln Lys Val Met Leu Val Cys Ile Phe
            180                 185                 190

Pro Gln Ile Leu Asn Arg Tyr Phe
        195                 200

<210>  138
<211>  215
<212>  PRT
<213>  Homo sapiens

<400>  138

Gly Lys Glu Lys Ser Asp Tyr Phe Ser Thr Thr Ala Ile Phe Lys Leu
1               5                   10                  15

Leu Glu Ala Val Cys Ile Pro Ser Ser Glu Val Ser Gly Ser Ser Pro
            20                  25                  30

Cys Val Ala Glu Arg Arg Leu His Pro Ser Ser Leu Pro Lys Ala Thr
        35                  40                  45

Thr Ala Tyr Leu Arg Ile Thr Thr Ile Ser Cys Asp Pro Tyr Ile Ala
    50                  55                  60

Met Val Asn Leu Ser Ile Asp Leu Tyr Tyr Ile Met Gly Leu Gln Gln
65                  70                  75                  80

Phe Cys Lys Leu Asp Glu Asp Phe Tyr Lys Glu Tyr Trp Arg Leu Gly
                85                  90                  95

Glu Val Thr Cys Asp Gly His Ile Pro Gly Ser Met Tyr Thr Ile Ser
            100                 105                 110

Leu Leu Gly Leu Cys His Thr Val Leu Ser Cys Ser Trp Gly Asn Ile
        115                 120                 125

Ser Gly Thr Cys Leu Ile Arg Val Val Cys Cys Gly Gln Gln Arg Asp
    130                 135                 140

Gly Cys Val Ser Gly His Leu Pro His Thr Gln Val Pro Leu Arg Thr
145                 150                 155                 160

Leu Ala Leu Thr Leu Lys Asn Gln Leu Val Val Cys Leu Gln Arg Asn
                165                 170                 175

Cys Phe Gln Gly Pro Phe Ser Ala Leu Thr Phe His Gln Val Ser Pro
            180                 185                 190
```

```
Leu Ala Pro Ala Gln Ser Ser Lys Ile Phe Leu Thr Thr Pro Val Ser
        195                 200                 205

Asp Val His Gln Met Leu Ile
    210                 215

<210>  139
<211>  163
<212>  PRT
<213>  Homo sapiens

<400>  139

Gly Trp Lys Asp His Ser Asp Thr Val Ala Gly Ala Cys Trp Glu Gln
1               5                   10                  15

Glu Trp Lys Gln Gly Trp Asp Phe Ser Leu Gln Pro Thr Ile Met Val
            20                  25                  30

Leu Thr Ser Leu Val Leu Ala Gly Leu Thr Cys Phe Ser Ala Arg Gly
        35                  40                  45

Ala Leu Gly Asn Gln Ser Ala Glu Asp Thr Cys Ser Ser Val Phe Thr
    50                  55                  60

Pro Tyr Trp Gln Leu Ser Trp Cys Asn Ala Leu Asp Trp Ala Leu Gly
65                  70                  75                  80

Arg Leu Asn Gln Ser Ser Pro Arg Thr Gly Asn Phe Leu Gly Ala Met
                85                  90                  95

Pro Leu Thr Gly His Trp Glu Gly Cys Lys Asn Ser Phe Cys Pro Gln
            100                 105                 110

Glu Glu Gln Arg Val Gly Leu His Pro Asp Asn Cys Pro Thr Asn Gly
        115                 120                 125

Met Cys Arg Pro Gly Gly Ala Gly Ala Val Ala Leu Met Leu Phe Pro
    130                 135                 140

Val Leu Leu Glu Gly Gly Ser Met Pro Trp Arg Gln Leu His Gly Ser
145                 150                 155                 160

Trp Gly Ser


<210>  140
<211>  194
<212>  PRT
<213>  Homo sapiens

<400>  140

Ile Met Ile Asp Arg Asp Val Gln Pro Phe Gly Asp Leu Arg Ala Gln
1               5                   10                  15

Pro Gly Glu Gln Gly Val Ser Glu Val Leu Leu Ser Thr Ala Ile Leu
            20                  25                  30

Asn Ser Pro Asn Leu Gln Pro Gly Pro Leu Ser Phe His Glu Leu Thr
        35                  40                  45

Ser Gln Pro Leu Phe Cys Cys Leu Trp Arg Lys Asn Asp Val Val Lys
    50                  55                  60
```

```
Thr Phe Glu Asn Gln Asp Leu Asn Asn Lys Phe Ile Ala Arg Cys Phe
65                  70                  75                  80

Pro Ile Gly Lys Lys Glu Tyr Met Asn Glu Ile Gln Leu Ser Thr Ser
                85                  90                  95

Ala Asn Ser Thr Asp Ser Glu Phe Lys Gly Pro Phe Pro Ala Leu Ser
            100                 105                 110

Leu Met Thr Leu Thr Gly Cys Phe Ser Leu Ser Trp Leu His Leu Met
        115                 120                 125

Gly Ala Ser Trp His Leu Leu Cys Gly Gln Gly Val Glu Lys Thr Pro
    130                 135                 140

Pro Ala Val Asn Ser Leu Thr Val Asn Ile Cys Val Asn Ile Cys Leu
145                 150                 155                 160

Glu Asp Leu Ser His Thr Pro Thr Ile Leu Thr Asn Ile Lys Gly His
                165                 170                 175

Gly Asp Glu Ser Leu Asn Ser Ala Pro Ser Leu Pro Leu Gln Gly Gln
            180                 185                 190

Met Cys
```

<210> 141
<211> 320
<212> PRT
<213> Homo sapiens

<400> 141

```
Tyr Leu Phe Leu His Ser Gln Arg Ser His Gln Lys Gln Pro Val Leu
1               5                   10                  15

Cys Ser Gln Ser Gln Thr Asn Ala Lys Ala Leu Lys His Lys Arg Ser
            20                  25                  30

Gln Glu Val Ser Ala Asn Leu Asp Leu Lys Thr Asn His Ile Val Ile
        35                  40                  45

Gly Trp Gly Lys Val Ile Ile Pro His Arg Ser Tyr Val Pro Thr Gly
    50                  55                  60

Thr Ile Thr Glu Asn Lys His His Arg Gly Trp Met Thr Phe Glu Ser
65                  70                  75                  80

His Asn Ala Lys Leu Glu Leu Gly Leu Lys Pro Lys Phe Leu Ala His
                85                  90                  95

Arg Ser Ser Asp Pro Pro Ile Pro His Ala Ile Pro Gly Ser Leu Leu
            100                 105                 110

Leu Gly Phe Phe Ser Ala Glu Glu Arg Asn Ser Gly Phe Gln Lys Leu
        115                 120                 125

Leu Ala Thr Leu Pro Phe Thr Val Tyr Ser Gln Trp Glu Glu Gly Leu
    130                 135                 140

Leu His Ser Ser Leu Leu Ser Pro Glu Arg Arg Leu Pro Gln Ala Cys
145                 150                 155                 160

Ile Trp Gly Lys Gln Ala Gly Ser Ala Val Val Lys Ser Thr Ala Pro
```

165 170 175

Gln Gln Ser Glu Arg Ser Val Ser Asn Leu Gln Ala Met Gln Pro Lys
180 185 190

Ser Gln Tyr Pro Ser Leu Tyr His Glu Asp Asn Thr Gly Thr Asn Phe
195 200 205

Leu Gly Val Leu Ala Phe Asn Gly Cys His Met Arg Cys Leu Ala Pro
210 215 220

Ser Lys Pro Thr Asp Ala Asp His Phe Thr Val His Arg Lys Leu Ser
225 230 235 240

Lys Ile His Pro Ala Leu Ser Gly Asn Val Leu Val Ile Ser Leu Ser
245 250 255

Thr His Ile Ile Thr Lys Ser Glu Ser Lys Tyr Ser Arg Ala Leu Asn
260 265 270

Pro Thr Thr Leu Met Ser Leu Leu Arg Gly Gly Arg Asp Val Ala Phe
275 280 285

Leu His Cys Asn Ser Gln Phe Gln Tyr Ser Ile Phe Phe Phe Arg Asn
290 295 300

Phe Cys Ile Gln Leu Thr Val Leu Val Arg Arg Ala Glu Gly Glu Gly
305 310 315 320

<210> 142
<211> 310
<212> PRT
<213> Homo sapiens

<400> 142

Lys Leu Ser Asn Thr Gln Lys Lys Ser Arg Ile Ile Glu His Arg Leu
1 5 10 15

Ile Ala Thr Ile Leu Ser Arg Ile Ile Ala Val Cys Asp Asn Phe Phe
20 25 30

Val Ser Ile Phe Asp Cys Ile Phe Ser Met Thr Lys Ser Asn Ser Arg
35 40 45

Glu Gly Gln Ser Trp Phe Tyr Ser Pro Phe Tyr Arg Gln Asn Leu Ala
50 55 60

Gln Cys Leu Leu Tyr Thr Met Phe Gln Leu Tyr Ile Cys Met Asn Phe
65 70 75 80

Ile Ile Ile Pro Lys Met His Val Leu Ala Val Gln Tyr Tyr Lys Lys
85 90 95

Ile Leu Val Val His Leu Lys Gly Asn His Phe Phe Leu Leu Gln Ala
100 105 110

Ile Ile Thr Asn Leu Phe Arg Ala Leu Gln Met Ile Lys Ala Leu Tyr
115 120 125

Leu Ser Ile Ile Ile Arg Ile Thr Leu Leu Phe Ile Gln Leu Ser Ser
130 135 140

Ile Pro Ser Ser Val Ser Phe Arg Lys Ser Phe Gly Gly Glu Phe Asn
145 150 155 160

```
Thr Val Gly Arg Lys Leu Leu Gly Met Tyr Asn Ile Ser Phe Ser Val
                165                 170                 175

Ile Lys Tyr Asn Phe Cys Trp Asn Ala Phe Ala Ser Ser Leu Val Lys
            180                 185                 190

Ile Leu Phe Asn Ser Pro Ile Cys Ser Asp Phe Asp Met Leu Thr Trp
        195                 200                 205

Leu Gly Tyr Ser Pro Gln Leu Leu Asn Gln Met Ile Ile Gln Leu Phe
    210                 215                 220

Leu Pro Phe Ala Asp Val Ile Gln Ser Thr Thr Ser Ile Trp Val Lys
225                 230                 235                 240

Lys Phe Arg Ile Tyr Val Cys Ile Leu Trp Val Gly Leu Ile Gln Ser
                245                 250                 255

Val Gly Arg Leu Lys Lys Gln Gly Ser Leu Ser Gln Lys Glu Lys Ile
            260                 265                 270

Val Cys Leu Trp Ile Lys Ala Leu Ala His Thr Cys Val Ser Ala Ser
        275                 280                 285

Gln Ile Ser Asp Cys Leu Ala Ser Pro His Ile His Val Ser Gln Phe
    290                 295                 300

Leu Lys Ile Asn Leu Leu
305                 310

<210>  143
<211>  316
<212>  PRT
<213>  Homo sapiens

<400>  143

Leu Gly Ile Cys Ser Phe His Phe Ser Tyr Cys Leu Thr Ser Leu Leu
1               5                   10                  15

Tyr Phe Leu Leu Ser Phe Phe Thr Phe Gln Ser Ser Leu Ile His Ser
            20                  25                  30

Leu Ala Gly Phe Asn Leu Ala Leu Pro Tyr Ser Leu Ser Phe Leu Asn
        35                  40                  45

Lys Tyr Leu Asn Phe Tyr Val Thr Phe Lys His Phe Leu Cys Asn Leu
    50                  55                  60

Leu Leu Thr His Thr Glu Ile Leu Leu Lys Val Leu Ser Cys Tyr Ile
65                  70                  75                  80

Leu Lys Val Ser Val Cys Ser Leu Phe Phe Pro Arg Asp Asn Cys Phe
                85                  90                  95

Phe Thr Phe Tyr Ile Ser Phe Phe Leu Cys Phe Gln Phe Phe Gln Leu
            100                 105                 110

Tyr Tyr Lys Lys Phe Gln Thr Glu Asn Leu Asn Lys Trp Tyr Asn His
        115                 120                 125

Arg Asn Phe Leu Arg Phe Asp Tyr Leu Phe Val Phe Ala Phe Leu Phe
    130                 135                 140
```

```
Leu Cys Met Leu Ile Ser Ile Thr Pro Phe Glu Val Lys Phe Pro Ser
145                 150                 155                 160

Asn Gln Arg Lys Asn Ser Gly Tyr Phe Ile Gly Arg Gly Thr Gly Glu
                165                 170                 175

Pro Ser Lys Ala Ser Gly Asn Val Leu His Leu Asn Leu His Gly Ser
            180                 185                 190

Tyr Thr Cys Lys Asn Ser Glu Arg Tyr Thr Ser Asp Leu Tyr Pro Leu
        195                 200                 205

Leu Cys Ile Ser Ser Ile Ser Lys Lys Arg Gly Phe Ala Gly Glu Val
    210                 215                 220

Ala Val Ile Leu Thr Leu Tyr Ser Ile Leu Ile His Val Ile Pro Lys
225                 230                 235                 240

Asn Lys Asp Ile Leu Leu Tyr Asn Tyr Val Thr Ile Leu Thr Phe Lys
                245                 250                 255

Asn Val Asn Ser Ile Thr Ile Cys Ser Ile Gln Ser Met Leu Lys Ile
            260                 265                 270

Ser Gln Val Pro Arg Met Ile Leu Pro Pro Ser Gly Leu His Thr Ala
        275                 280                 285

Phe Gly Cys Tyr Val His Leu Val Leu Tyr Ser Val Glu Ser Pro Thr
    290                 295                 300

Phe Leu Leu Ser Lys Thr Leu Thr Tyr Gln Gly Val
305                 310                 315
```

<210> 144
<211> 204
<212> PRT
<213> Homo sapiens

<400> 144

```
Glu Ile Ile Arg Val Tyr Pro Leu Thr Ser Ser Pro Ser Gly Asn Ile
1               5                   10                  15

Leu Gln Asn Asn Gly Thr Gly Ser Pro Gly Tyr His Gln Ser Gln Gly
            20                  25                  30

Ser Tyr Arg Thr Ala Leu Leu Pro Gln Gly Ser Leu Cys Trp Leu Phe
        35                  40                  45

Ile Thr Thr Val Arg Met Leu Leu Pro Leu Leu Asn Tyr Gln Gln Pro
    50                  55                  60

Leu Ile Cys Ser Ser Phe Leu Gln Cys His Phe Asn Ser Val Val Met
65                  70                  75                  80

Glu Ser Met Leu Tyr Ile Thr Phe Trp Asp Trp Leu Phe Ser Leu Cys
                85                  90                  95

Ile Ile Pro Ser Arg Ser Ile Lys Trp Leu Ser Met Val Val His Ser
            100                 105                 110

Val Ser Leu Val Ser Lys Ser Asp Leu Phe Gln Val Asn Ile Gly Ser
        115                 120                 125

His Cys Ser Thr Ala Ser Leu Ser Ser Ser Pro Trp Asn Asp Ser Gln
```

```
    130                 135                 140

Ala Pro Cys Thr Gly Thr Leu Thr Pro Ala Trp Leu Ser Ser Leu His
145                 150                 155                 160

Ala Ile Arg Ser Leu Leu Val Cys Phe Ala Pro Val Thr Trp Val Ser
                165                 170                 175

Cys Gln Tyr Ile Asn Ser Gln Cys Phe Ser Ala Tyr Pro Ser Ser Pro
            180                 185                 190

Thr Leu Val Phe Asp Phe Thr Val Ser Ser Ala Trp
        195                 200

<210>  145
<211>  99
<212>  PRT
<213>  Homo sapiens

<400>  145

Phe Leu Phe Glu Lys Ser His Cys Thr Glu Tyr Ile Asn Glu Phe Ser
1               5                   10                  15

Glu Asp Ile Cys Val Lys Ser Gly Leu Ser Gly Thr Val Cys Leu Lys
            20                  25                  30

Leu Trp Lys Glu Ile Leu Phe Phe Phe Ser Ala Phe Val Ser Ser Asn
        35                  40                  45

Phe Leu Ile Val Ile Ser Gln Gly Pro His Arg Cys Ile Trp Ala Thr
    50                  55                  60

Gly Phe Phe Cys Phe Phe Phe Phe Thr Cys Cys Leu Ser Ile Pro Asn
65                  70                  75                  80

Arg Gly His Gln Ile Pro Gly His Leu Val Val Leu Val His Gly Leu
                85                  90                  95

Leu Gly Thr


<210>  146
<211>  57
<212>  PRT
<213>  Homo sapiens

<400>  146

Thr Val Phe Asn Glu Glu Phe Trp Gln Ala Phe Pro Pro Ile Val Pro
1               5                   10                  15

Phe Arg Lys Ala Ser Ser Tyr Ser Val Met Thr His Val Ile Phe Cys
            20                  25                  30

Val Leu Pro His Arg Asp Cys Leu Phe Phe Phe Leu Phe Ser Glu Thr
        35                  40                  45

Trp Ile Asn Ser Trp Tyr Leu Glu Ser
    50                  55

<210>  147
<211>  192
<212>  PRT
<213>  Homo sapiens
```

<400> 147

```
Val Cys Phe Val Ile Ile Ser Phe Phe Leu Trp Val Leu Pro Leu Val
1               5                  10                  15

Val Leu Val Cys Leu Pro Gly Lys Phe Leu Thr Leu Ala Phe Asp Leu
            20                  25                  30

Leu Leu Leu Leu Ser Ile Val Val Ser Met Pro His Leu Val Ile Tyr
        35                  40                  45

Phe Leu Ala Glu Leu Tyr Arg Lys Arg His Arg Glu Ser Leu Lys Ala
    50                  55                  60

Val Phe Gln Arg Ala Leu Leu Ser Glu Met Glu Ala Trp Ile Lys Gly
65                  70                  75                  80

Val Ser Gly Pro Arg Ser Gln Gly Arg Phe Gln Pro His Ser Trp Lys
                85                  90                  95

Gln Thr Ala Leu Leu Gly Gly Ser Ala Pro Pro Gln Arg Gln Gly Leu
            100                 105                 110

Pro Met His Lys Ala Val Lys Gly Ile Met Ser Gly Lys His Ala Glu
        115                 120                 125

Ser Ser Lys Glu Gln Gly Glu Cys Ser Asp Tyr Leu Leu Pro Leu Cys
    130                 135                 140

Ile Phe Arg Val Thr Arg Phe Leu Thr Glu Phe Lys Thr Lys Leu Leu
145                 150                 155                 160

Cys Phe Cys Pro Ile Ile Leu Asn Ser His Gly Asn Pro Leu Glu Arg
                165                 170                 175

Gln Val Arg Ser Lys Ala Asp Leu Pro Gly Phe Phe Phe Phe Phe Phe
            180                 185                 190
```

<210> 148
<211> 122
<212> PRT
<213> Homo sapiens

<400> 148

```
Ile Gly Phe Ser Leu Pro Leu Leu Leu Leu Lys Ile Val Leu Ile Gly
1               5                  10                  15

His Phe Leu Leu Lys Pro Arg Pro Leu Trp Lys Cys Gly Ala Tyr Arg
            20                  25                  30

Glu Val Arg Arg Pro Arg Ser Ala Ala Arg Thr Arg Arg Pro Leu Thr
        35                  40                  45

Arg Val Cys Ala Ser Cys Glu Lys Ala Phe Leu Ala Ser Leu Asn Ala
    50                  55                  60

Cys Phe Thr Cys Ser Leu Phe Leu Ile Ser Phe Pro Asn Cys Val Pro
65                  70                  75                  80

Ser Ile Leu Leu Tyr Cys Ser Leu Cys Trp Glu Gly Arg Tyr Glu Asn
                85                  90                  95

Val Ala Tyr Ile Lys Thr Ala Glu Ser Cys Ile Leu Cys Cys Pro Glu
```

100 105 110

Ser Arg Asn Thr Val Leu Leu Leu Ala Val
115 120

<210> 149
<211> 114
<212> PRT
<213> Homo sapiens

<400> 149

Leu Ser Pro Asp Thr Ile Arg Met Asn Ala Asp Cys Cys Ile Ser Gly
1 5 10 15

Met Trp Leu Thr Ala Ala Ala Thr Cys Leu Gln Glu Cys Pro Cys Leu
20 25 30

Val Ser Val Thr Arg Cys Ser Val His Leu Asp Gln Tyr Ile Thr Phe
35 40 45

Thr Asn Val Ser Glu Arg Asn Val Arg Ile Asn Gln Asp Ile Ser Leu
50 55 60

Leu Val Phe Phe Phe Trp Gln Ala Ala Leu Thr Ile Val Leu Glu Pro
65 70 75 80

Thr Pro Tyr Val Asn Ile Ile Gln Ser Ser Ile Ser Lys Ala Gly Ser
85 90 95

Gln Glu Met Leu Phe Ile Arg Arg His Ile Gly Tyr Ser Leu Gln Asn
100 105 110

Val Lys

<210> 150
<211> 235
<212> PRT
<213> Homo sapiens

<400> 150

Met Val Pro Met Ser Pro Leu Arg Cys Arg Leu Asn Pro His Thr Thr
1 5 10 15

Leu Gly Val Val Val His Ala Phe Pro Tyr Ser Ser Gly Asp Gln Asn
20 25 30

Cys Ile Gly Pro Val Arg Arg Gly Thr Trp Ile Leu Glu Ser Asn Lys
35 40 45

Pro Phe Ser His Phe Leu Val Gly Pro Ala Ser Lys Leu Thr Phe Leu
50 55 60

Ser Leu Ser Ser Ser Ile Lys Trp Glu Lys Leu His Leu Leu His Gly
65 70 75 80

Thr Ala Ile Arg Phe Lys Ile Met Val Ile Asn Asn Leu Val Gln Tyr
85 90 95

Leu Val Tyr Thr Lys Cys Ser Ile Asn Ala Thr Ala Ile Cys Ser Ser
100 105 110

His Pro Ile Leu Phe Phe Val Asp Asn Arg Phe Asn Ser Leu Ser Ile

```
        115                 120                 125

Lys Pro Gly Lys Lys Arg Asp Glu His Arg Pro Trp Ser Arg Ser Ile
    130                 135                 140

Lys Asp Ser Lys Gly Phe Ser Ser Gly His Pro Phe Pro Met Cys Trp
145                 150                 155                 160

Pro Asn His Val Pro Leu Trp Ser Ser Arg Leu Tyr Gly Leu Phe Asn
                165                 170                 175

Ser Thr Lys Ala Gln Val Asn Ile Pro Thr Pro Ser Asn Met Ser Thr
            180                 185                 190

Gly Pro Val Gly Asn Ser Val Ala Gly Gln Ala Leu Cys Ser Val Ser
        195                 200                 205

Ala His Gly Leu Ser Thr His Pro Asp Gln Pro Pro Val Leu Thr Ala
    210                 215                 220

Phe Leu His Gln Ile Leu Thr Ser Asn His Pro
225                 230                 235

<210>  151
<211>  202
<212>  PRT
<213>  Homo sapiens

<400>  151

Met Leu Gly Gly Pro Gly His Gly Gly Leu Ala His Arg Gly Ser His
1               5                   10                  15

Trp Glu Ile Gly Asn Leu Phe Phe Ala Gly Pro Asp Gln Tyr Ile Pro
            20                  25                  30

Leu Val Leu Gly Glu Pro Ser Gln Pro Pro Asn Ser Ser Trp Pro Leu
        35                  40                  45

Ser Gln Asn Gly Thr Asn Thr Glu Ala Thr Pro Ala Thr Asn Leu Thr
    50                  55                  60

Phe Ser Ser Tyr Tyr Gln His Thr Ser Pro Val Ala Ala Met Phe Ile
65                  70                  75                  80

Val Ala Tyr Ala Leu Ile Phe Leu Leu Cys Met Val Gly Asn Thr Leu
                85                  90                  95

Val Cys Phe Ile Val Leu Lys Asn Arg His Met His Thr Val Thr Asn
            100                 105                 110

Met Phe Ile Leu Asn Leu Ala Val Ser Asp Leu Leu Val Gly Ile Phe
        115                 120                 125

Cys Met Pro Thr Asn Pro Leu Asp Asn Leu Ile Thr Gly Glu Cys Gly
    130                 135                 140

Gln Leu Ala Ala Gly Val Ser Pro Thr Pro His Phe Asn Phe Ser Asp
145                 150                 155                 160

Lys Ala Gly Asn Gln Ser Leu Glu Asp Arg Tyr His Cys Trp Ala Gly
                165                 170                 175

Leu Leu Ala Met Pro Trp Tyr Ser Asn Ser Ser Arg Gln Ser Trp Gly
            180                 185                 190
```

Arg Val Arg Leu Val Asn Lys Arg Phe Asn
195 200

<210> 152
<211> 176
<212> PRT
<213> Homo sapiens

<400> 152

Met Leu His Leu Lys Val Thr Lys Leu Cys Val His Ile His Ile Ala
1 5 10 15

Asn Pro Pro Lys Leu Met Ser Leu Leu Trp Phe Gly Tyr Gly Leu Phe
20 25 30

Ile Pro Thr Lys Ile His Ile Glu Ile Ser Ser Pro Val Cys Trp Glu
35 40 45

Val Gly Pro Ser Trp Gly Met Ala Trp Cys His Ser Leu Gly Ser Gly
50 55 60

Val Leu Ala Val Ala Arg Met Asn Phe Leu Arg Glu Ile Leu Asn Ser
65 70 75 80

Ser Cys Gln Ser Glu Phe Leu Ser Gln Asp Ala Pro Trp Val Leu Ser
85 90 95

Leu Phe Thr Cys Pro Leu Ser Leu Pro Ser Leu Leu Cys Phe Asp Leu
100 105 110

Ala Asp Leu His Gln Lys Pro Ser Arg Cys Gln His Arg Ala Ser Leu
115 120 125

Thr Phe His Leu Gln Asn Cys Glu Leu Asn Lys Pro Leu Phe Phe Ile
130 135 140

Asn Tyr Leu Ala Ser Val Phe Cys Tyr Ser Asn Thr Lys Trp Thr Lys
145 150 155 160

Thr Val Ser Gln Thr Asn Cys Gly Leu Phe Leu Lys Val Thr Pro Thr
165 170 175

<210> 153
<211> 252
<212> PRT
<213> Homo sapiens

<400> 153

Leu Asn Thr Glu Cys Gln His Glu Pro Glu Val Met Leu Val His Gly
1 5 10 15

Arg Phe Leu Ser Asn Val Ile Leu Ser His Gln Val Thr Ala Ala Met
20 25 30

Ser Lys Ile His Lys Tyr Ser Ala Cys Lys Pro Lys Arg Pro Val Val
35 40 45

Leu His Pro Thr Cys Phe Leu Phe Val Trp Phe Gly Tyr Met Phe Cys
50 55 60

Leu Gly Ile Asn Cys Leu Leu Tyr Asn Leu Pro Gly Ser Leu Ser Ile
65 70 75 80

Leu Pro Leu His Pro Lys Leu Gly Ser Leu Asn Pro Tyr Ile Lys Phe
85 90 95

Ile Ser Pro Val Asn Ser Ala Ser Ile Leu Ile Phe Thr Ala Phe Leu
100 105 110

Ser Ala Ala Leu Ile Lys Phe Asn Ile Phe Glu Val Asp Tyr Pro Leu
115 120 125

Pro Tyr Phe Pro Pro Thr Thr Lys Ala Leu Gln Leu Leu Leu Tyr Ser
130 135 140

Ala Glu His Arg Trp Glu His Arg Cys His Ile Thr Ala Glu Ile Ser
145 150 155 160

Ile Leu Val Arg Thr His Pro Asp Ser Asp Met Lys His Ile Val His
165 170 175

Thr Thr Ile Ala His Arg Phe His Gln Glu Met Ser Ala Asp Ser Asp
180 185 190

Glu Gly Pro Thr Thr Pro Ser Gly Trp Arg Val Leu Asp Ser Ser Leu
195 200 205

Ser Pro Leu Pro Thr Pro Phe His Val Pro Ala Ser Gln His Glu Ala
210 215 220

Ala Ser Gln Gln Cys Gln Arg Thr Thr Asp Arg Pro Arg Thr Asn His
225 230 235 240

Ile His Pro Trp Lys Arg Ser Ser Val Tyr Tyr Met
245 250

<210> 154
<211> 205
<212> PRT
<213> Homo sapiens

<400> 154

Lys Leu Ser Pro Trp Gly Ser Ser Leu Trp Asn Val Asn Ile Ser His
1 5 10 15

Leu Ile Val His Phe Leu Lys Ser Lys Tyr Met Asp Lys Val Tyr Ala
20 25 30

Phe Pro Thr Glu Val Tyr Arg Gly Val Ile Lys Phe Ala Tyr Lys Ile
35 40 45

Phe Leu Asn Tyr Asp Leu Gly Arg Asp Val Val Val Ile Glu Ile Ile
50 55 60

Phe Trp Asn Cys Lys Ser Asn Met Tyr Asn Tyr Leu Ala Val Leu Pro
65 70 75 80

Ala Leu Ser Leu Thr Leu Pro Ile Ser Gly Ser Phe Leu Leu Ile Gly
85 90 95

Phe Gln Asp Lys Lys Cys Phe Leu Arg Asp Gly Phe Cys Val His Leu
100 105 110

Phe Lys Arg Ser Pro Leu Ser Ser Cys His Leu Leu Thr Asn Tyr His
115 120 125

```
Val Tyr Ser Leu Leu Trp Phe Gly Tyr Gly Leu Leu Val Pro Thr Lys
    130                 135                 140

Ser Tyr Val Glu Ile Met Ile Ser Arg Val Val Val Leu Gly Gly Gly
145                 150                 155                 160

Ala Glu Val Leu Ala Ser Trp Gly Gln Ile Pro Cys Lys Trp Leu Gly
                165                 170                 175

Ala Ile Leu Met Gly Val Asn Glu Phe Leu Leu Phe Asp Trp Val Ala
            180                 185                 190

Ser Gly Lys Gly Ile Ser Leu Pro Pro Ser Gly Leu Val
        195                 200                 205
```

<210> 155
<211> 113
<212> PRT
<213> Homo sapiens

<400> 155

```
Val Ser Gly His Phe Phe Trp Ser Cys Gly Phe Lys Val Ser Thr Thr
1               5                   10                  15

Leu Leu Ile Val Asp Lys Asn Gly Ser Met Trp Val Tyr Ile Leu Ile
            20                  25                  30

Trp Ser Cys Ser Tyr Ser Lys Ala Val Glu Ala Arg Ser His Ser Phe
        35                  40                  45

His Asp Ile Leu Met Ser Ser Leu Gly Arg Val Val Gly Val Val Ile
    50                  55                  60

Val Ser Gly Asp Lys Trp Gln Arg Leu Thr Gln Tyr Ser Phe Cys Leu
65                  70                  75                  80

Thr Ala Glu Phe Lys Pro Phe His Leu Leu Leu Val Leu Ser Thr Arg
                85                  90                  95

Gly Arg Lys Tyr Lys Leu Asp Cys Ala Leu His Arg Leu Tyr Ile Ile
            100                 105                 110

Ile
```

<210> 156
<211> 181
<212> PRT
<213> Homo sapiens

<400> 156

```
Leu Leu Tyr Leu Ser Leu Tyr Ile Tyr Gln Asp Leu Ser Arg Pro Pro
1               5                   10                  15

Gly Tyr Pro His Phe Val Asn Asp Pro Val Trp Ser Ser Ile Cys Gln
            20                  25                  30

Ala Val Gly Asn Arg Ala Leu Val Ser Val Phe Ser Phe Cys Asp Ala
        35                  40                  45

Gly Ser Pro Val Leu Thr Gln Asp Leu Leu Met Gly Arg Thr Tyr Val
    50                  55                  60
```

```
Pro Ser Arg Glu Ala Cys Gly Arg Glu Phe Leu Pro Ser Arg His Leu
65                  70                  75                  80

Leu Trp Phe Gly Tyr Gly Leu Cys Gly Pro Thr Lys Phe His Val Gly
                85                  90                  95

Ile Cys Pro Pro Ser Ile Gly Gly Thr Ala Trp Trp Glu Leu Phe Gly
            100                 105                 110

Leu Trp Glu Trp Ile Val Tyr Glu Cys Leu Gly Ala Ile Leu Met Arg
        115                 120                 125

Val Asn Ser Cys Lys Asn Trp Leu Leu Lys Arg Ala Trp His His Leu
    130                 135                 140

Leu Ser Leu Leu Ala Phe Leu Ser Tyr His Val Leu Ser Val Tyr Ala
145                 150                 155                 160

Ser Ser Leu His Leu Pro Pro Arg Val Glu Ala Ser Gly Phe Ile Arg
                165                 170                 175

His Arg Tyr Trp Cys
            180

<210>  157
<211>  190
<212>  PRT
<213>  Homo sapiens

<400>  157

Lys Lys Leu Val Arg Asp Cys Val Gly Asp Leu Cys Met Ala Gln Lys
1                5                  10                  15

Cys Pro Leu Ser Ile Leu Tyr Lys Leu Lys Thr Thr Asn Leu Asn Phe
            20                  25                  30

Val Leu Cys Ser His Gln Ser Leu Thr Val Ser Pro Leu Phe Ala Ser
        35                  40                  45

Tyr Val Lys Gly Thr Ile Phe Phe Glu Arg Cys Gln Asp Phe Ser Met
    50                  55                  60

Leu Cys Phe Thr Leu Phe Trp Phe Cys Met Leu His Phe Arg Gln Arg
65                  70                  75                  80

Ala Ala Val Lys Ser Tyr Arg Lys Ala Val Lys Thr Pro Trp Asn Tyr
                85                  90                  95

Phe Tyr Phe His Phe Ile Leu Ala Asp Pro Ala Tyr Ile Tyr Leu Phe
            100                 105                 110

Ile Thr Cys Leu Asn Val Glu Ser Phe Trp Val Ala Leu Ala Leu Asn
        115                 120                 125

Glu His Leu Glu Arg Ala Leu Ile Pro Ala Trp Ile Ile Ala Leu Leu
    130                 135                 140

Leu Pro Arg Ile Leu Thr His Phe Pro His Leu Arg Glu Val Leu Lys
145                 150                 155                 160

Phe Leu Arg Pro Arg Phe Val Ser Glu Cys Val Ile Met Gly Thr Asn
                165                 170                 175

Glu Ile Met Phe Ile Arg Gly Phe Val Phe Phe Ile Val Val
```

180 185 190

<210> 158
<211> 221
<212> PRT
<213> Homo sapiens

<400> 158

Ala Ser Leu Ala Cys Asn Ala Ser Leu Leu Pro Ser Leu Pro Tyr Phe
1 5 10 15

Glu Thr Phe Asn Cys Leu Leu Ala Leu Tyr His Thr Phe Ser Tyr Ile
20 25 30

Thr Phe Phe Ile Gly Leu Ser Leu Leu Tyr Leu Ser Leu Tyr Ile Tyr
35 40 45

Gln Asp Leu Ser Arg Pro Pro Gly Tyr Pro His Phe Val Asn Asp Pro
50 55 60

Val Trp Ser Ser Ile Cys Gln Ala Val Gly Asn Arg Ala Leu Val Ser
65 70 75 80

Val Phe Ser Phe Cys Asp Ala Gly Ser Pro Val Leu Thr Gln Asp Leu
85 90 95

Leu Met Gly Arg Thr Tyr Val Pro Ser Arg Glu Ala Cys Gly Arg Glu
100 105 110

Phe Leu Pro Ser Arg His Leu Leu Trp Phe Gly Tyr Gly Leu Cys Gly
115 120 125

Pro Thr Lys Phe His Val Gly Ile Cys Pro Pro Ser Ile Gly Gly Thr
130 135 140

Ala Trp Trp Glu Leu Phe Gly Leu Trp Glu Trp Ile Val Tyr Glu Cys
145 150 155 160

Leu Gly Ala Ile Leu Met Arg Val Asn Ser Cys Lys Asn Trp Leu Leu
165 170 175

Lys Arg Ala Trp His His Leu Leu Ser Leu Leu Pro Phe Ser Pro Thr
180 185 190

Met Cys Ser Ser Val Tyr Ala Ser Ser Leu His Leu Pro Pro Arg Val
195 200 205

Glu Ala Ser Leu Arg Leu His Gln Thr Gln Ile Leu Val
210 215 220

<210> 159
<211> 156
<212> PRT
<213> Homo sapiens

<400> 159

Phe Leu Ser Cys Trp Thr Gln Lys Arg Leu Pro Ser Arg Glu Thr Cys
1 5 10 15

Pro Gln Leu Phe Trp Val Lys Ala Cys Ala Gly Thr Tyr Asp Ser Lys
20 25 30

Ser Gln Leu Lys Trp Ile Ser Ile Ser Ser Ser Ser Asn Ser Pro Ser

```
        35                  40                  45

Leu Arg Lys Asn Ser Ser Phe Leu Cys Phe Ile Tyr Val Asn Ile Gly
    50                  55                  60

Lys Arg Cys Met Tyr Asp Val Phe Phe Leu Phe Ile Ser Phe Cys Ser
65                  70                  75                  80

Asn Cys Lys Lys Ser His Met Phe Leu Val Lys Lys Ser Thr Asn Gln
                85                  90                  95

Pro Thr Leu Lys Asn Leu Asn Asn Glu Gln Arg Glu Lys Lys Leu Pro
            100                 105                 110

Asn Ile Lys His Asn Val Tyr Thr Leu Gln Lys Leu Glu Lys Tyr Arg
        115                 120                 125

Lys Thr Gln Arg Lys Glu Lys Lys Ile Thr Ser Thr Gln Asn Tyr Phe
    130                 135                 140

Cys Phe Gln Tyr Ile Ala Lys His Phe Ser Met Tyr
145                 150                 155

<210>  160
<211>  200
<212>  PRT
<213>  Homo sapiens

<400>  160

Phe Val Lys Lys Val Gln Ser Met Asn Leu Thr Gly Lys Ser Pro Leu
1               5                   10                  15

Lys Ser Thr Cys Trp Leu Gly Asn Glu Lys Glu Val Glu Pro Gly Lys
            20                  25                  30

Ala Thr Pro Ser Gly Tyr Ile Gly Lys Glu Ile Lys Ala Ala Thr Thr
        35                  40                  45

Arg Gln Ser Glu Val Ala Gln Lys Trp Ser Met Phe Leu Arg Glu Leu
    50                  55                  60

Leu Trp Phe Gly Tyr Gly Leu Ser Val Pro Thr Lys Pro His Val Asp
65                  70                  75                  80

Ile Phe Phe Pro Val Trp Gln Cys Glu Val Arg Pro Ser Gly Arg Cys
                85                  90                  95

Leu Gly His Gly Gly Gly Ser Leu Met Asn Thr Cys Cys Ser Gln Val
            100                 105                 110

Ser Glu Phe Leu Trp Gln Asp Ile Ser Ser Cys Gly Asn Gly Val Val
        115                 120                 125

Ser Ser Arg Val Gly His Lys Ala Thr Cys Pro Ser His Val Ser Thr
    130                 135                 140

Ser Pro Leu Thr Phe Ser Thr Met Phe Trp Gln His Arg Ser Leu Thr
145                 150                 155                 160

Arg Ser Ala Asp Ala Gly Thr Met Val Leu Ile Gln Pro Ala Glu Gln
                165                 170                 175

Ala Lys Ile Tyr Phe Leu His Lys Leu Leu Ser Leu Arg Tyr Phe Phe
            180                 185                 190
```

```
Phe Phe Phe Leu Arg Gln Ser Leu
        195                 200

<210>  161
<211>  191
<212>  PRT
<213>  Homo sapiens

<400>  161

Gln Cys Gly Asp Ser Gly Ser Arg Arg Val Lys Asn Glu Val Trp Val
1               5                  10                  15

Gly Lys Glu Trp Ser Gly His Asp Arg Leu Trp Asn Leu Phe Glu Val
            20                  25                  30

Lys Leu Glu Val Leu Lys Asn Phe Asn Gln Ala Asn Gly Phe Leu Leu
        35                  40                  45

Phe Ile Leu Ile Lys Asp Tyr Phe Asp Cys Ser Val Glu Asn Arg Val
    50                  55                  60

Glu Arg Asn Arg Glu Val Arg Asn Leu Leu Leu Phe His Met Lys Met
65                  70                  75                  80

Met Tyr His Cys Leu Leu Ser Ala Trp Gly Leu Cys Arg Glu Lys Trp
                85                  90                  95

Pro Asn Ile Arg Tyr Lys Arg Glu Tyr Thr Cys Gln Asp Leu Leu Met
            100                 105                 110

Asp Tyr Ile Leu Val Leu Ile Val Asn Leu Gln Phe Leu Asn Gly Glu
        115                 120                 125

Leu Leu Leu Met Tyr Ala Val Phe Ile His Tyr Ser Arg Cys Val Leu
    130                 135                 140

Gln Met Thr Glu Ile Leu Lys Cys Asn Leu Ile Lys Asn Leu Leu Ile
145                 150                 155                 160

Ser His Ile Val Ser Tyr Asp Trp Glu Ile Gly Val Arg Thr Leu Gly
                165                 170                 175

Lys Ala Val Ser Gln Ala Tyr Arg Leu Leu Asn Leu Val Leu Ile
            180                 185                 190

<210>  162
<211>  76
<212>  PRT
<213>  Homo sapiens

<400>  162

Leu Val Ala Ala Ala Leu His Thr Arg Leu Pro Pro Pro Gln Gly Val
1               5                  10                  15

Pro Asp Cys Ser Pro Arg Pro Val Gln Gln Leu Glu Thr Met Ala Gly
            20                  25                  30

Arg Ile Arg Gly Arg Arg Ala Tyr Cys Ser Lys Thr Phe Gly Thr Ile
        35                  40                  45

Cys Phe Ile Pro Tyr Phe Phe Gln Leu His Cys Val Leu Leu Leu Leu
    50                  55                  60
```

```
Val Ile Phe Thr Lys Glu Asn Phe Phe Thr Leu Ile
65                  70                  75

<210>  163
<211>  155
<212>  PRT
<213>  Homo sapiens

<400>  163

Thr Pro Ala Trp Val Ile Glu Arg Asp Ser Val Ser Lys Lys Lys Arg
1               5                   10                  15

Lys Lys Lys Val Met Leu Val Glu Ala Asn Ser Arg Leu Ile Tyr Ile
            20                  25                  30

Phe Lys Asn Ile Phe Leu Gly Asn Leu Ile His Ile Gln Tyr Arg Leu
        35                  40                  45

Ser Ser Leu Ser Thr Leu Tyr Leu Ile Leu Pro Val Lys Leu Cys Thr
    50                  55                  60

Ile Lys Val Met Ser Cys Phe Ser Ala Met Pro His Ala Gly Gly Thr
65                  70                  75                  80

Ser Phe Leu Thr Pro Thr Ser Phe Pro Gly Glu Pro Arg Cys Ala Lys
                85                  90                  95

Gly Trp Asp Ala Trp His Arg Met Pro Ala Ser Arg Cys Leu Asn Ala
            100                 105                 110

Pro Ala Val Ser Pro Gly Ala Lys Ser Tyr Ser Thr Val Ser Leu Pro
        115                 120                 125

Pro Ala Glu Asn Arg Ser Ala Trp Cys Ile Gln Ala Thr Lys Gly Ile
    130                 135                 140

Cys Thr Asp Met His Thr Ala Ser Ala Val Gly
145                 150                 155

<210>  164
<211>  193
<212>  PRT
<213>  Homo sapiens

<400>  164

Gly Leu Ile Glu Trp Asn Leu Glu Ala Gly Arg Thr Gly Glu Gly Leu
1               5                   10                  15

Pro Val Phe Ala Ser Lys Val Ile Phe Ser Tyr Leu Cys Glu Val Leu
            20                  25                  30

Arg Asn Tyr Lys Asn His Pro Ser Tyr Tyr Lys Arg Asp Gln Asp Gln
        35                  40                  45

Gln His Phe Leu Lys His Arg Val Gly His Asp Lys Cys Pro Arg Arg
    50                  55                  60

Asp Asp Thr Arg Glu Glu Ser Gly Val Asn Leu Ser Val Leu Thr His
65                  70                  75                  80

Tyr Phe Ile Ser Asn Leu Leu Ala Ser Lys Ile Val Phe Phe Phe Cys
                85                  90                  95
```

Glu Ser Leu Ser Ser Phe Pro Leu Phe Thr Asn Asn Ser Tyr Pro Gln
100 105 110

Ser Leu Cys Leu Pro Ile Gly Cys Phe Leu Ser Lys Phe His Leu Gly
115 120 125

Leu Leu Leu Pro Pro Ser Arg Thr Leu Lys Ser Gln Ser Tyr Leu Ile
130 135 140

Gly Ser Leu Asn Ala Leu Cys Ile Phe Leu Val Thr Thr His Asn Asn
145 150 155 160

Tyr Asn Asp Lys Gln Lys Asn Phe Ile Ser Val Ser Leu Gly Glu Asp
165 170 175

Gly Trp Met Glu Pro Gln Lys Tyr Ala Arg Ile Thr Lys His Asn Leu
180 185 190

Asn

<210> 165
<211> 124
<212> PRT
<213> Homo sapiens

<400> 165

Phe Leu Ser Gly Ile Pro Leu Thr Gly Leu Arg Lys Ser Thr Gln Tyr
1 5 10 15

Ala Phe Leu Ser Ala Glu Asp Ser Asn Thr Ser Lys Ile Ile Leu Ile
20 25 30

Phe Leu Phe Ala Lys Val Tyr Leu Gln Lys Leu Phe Leu Gln Lys Leu
35 40 45

Lys Ser Arg Ser Gln Leu Ser Ile Phe Ile Val Leu Thr Ser Arg Leu
50 55 60

Thr Asn Gln Leu Leu Thr Pro Phe Pro Glu Lys Cys Phe Ala Leu Thr
65 70 75 80

Lys Val Glu Ile Leu Arg Leu Ile Cys Ser Ile Ser Trp Ile His Tyr
85 90 95

Ile Tyr Tyr Leu Ile Tyr Cys Ser Leu Val Val Cys Ile Cys His Tyr
100 105 110

Ser Glu Ile Gln Lys Lys Cys Ser Asn Leu Tyr Leu
115 120

<210> 166
<211> 230
<212> PRT
<213> Homo sapiens

<400> 166

Gln Leu Gly Ile His Thr Gln Ser Thr Gln Pro Gln Glu His Ser Lys
1 5 10 15

Gly Gln Glu Leu Lys Leu Thr Ser Arg Asp Gln His Leu Thr Lys Ser
20 25 30

```
His Val Met Asn Gln Lys Lys Lys Lys Lys Pro Lys Ser Lys Thr Phe
        35                  40                  45

Asp Asn Arg Met Trp Cys Trp Asp Met Arg Gln Thr Val Val Ile Tyr
    50                  55                  60

Ser Val Ile Tyr Arg Leu Pro Phe Thr Cys Arg Leu Ser Phe Tyr Phe
65                  70                  75                  80

Asn Gln Met Leu Phe Gln Val Ile Ser Thr Leu Val Asn Gln Val Leu
                85                  90                  95

Glu Ser Phe Ile Pro Arg Leu Cys Asn Thr Val Ile Ser Leu Ser Pro
            100                 105                 110

Phe Leu Gly Gln Ala Asn Ser Leu Leu Ile Ser Leu Gly Trp Ile Leu
        115                 120                 125

Lys Ser Asn Gln Ala Thr Asn Asp Leu Asp Cys Cys Tyr Phe Ser His
    130                 135                 140

Leu Ala Ser Tyr Phe Leu Pro Leu Tyr Val Leu Phe Leu Ile Leu Ile
145                 150                 155                 160

Leu Leu Phe Leu Lys Leu Val Lys Thr Ile Ser Pro Leu Gly Ser Leu
                165                 170                 175

His Leu Ile Pro Leu Pro Arg Ile Leu Cys Pro Pro Asp Ile Asn Met
            180                 185                 190

Val Tyr Tyr Phe Thr Ser Phe Glu Pro Ser Ser Asn Val Thr Phe Ser
        195                 200                 205

Ile Lys Pro Thr Met Leu Val Ile Phe Tyr His Phe Leu Ser Asp Met
    210                 215                 220

Ser Phe Ala Leu Tyr Cys
225                 230
```

<210> 167
<211> 192
<212> PRT
<213> Homo sapiens

<400> 167

```
Ile Thr Glu Asn Pro Phe Met Ala Ala Arg Arg Thr Trp Ile Phe Leu
1               5                   10                  15

Ile Phe His Trp Pro Trp Ser Gly Gly Thr Glu Pro Lys Ser Thr Trp
            20                  25                  30

Gly Ala Gly Lys Ala Ala Val Arg Gly Arg Pro Cys Trp Cys Trp Pro
        35                  40                  45

Cys Gln Pro Ala Leu Leu Val Ser Ile Ile Ala Leu Val Trp Gln Arg
    50                  55                  60

Thr Leu Cys Asp Cys Glu Leu Arg Ser Ala Leu Arg Ser Leu Gln Ala
65                  70                  75                  80

Ser Gly Leu Gln Val Pro Val Gln Pro Ser Ile Cys Phe Ser Pro Tyr
                85                  90                  95
```

```
Val Arg Ser Thr Pro Thr Pro Val Tyr Thr Gly Ala Lys Cys Leu Leu
            100                 105                 110

Arg Phe Trp Ala Phe His Gly Lys Val Leu Asn Val Phe Lys Tyr Leu
        115                 120                 125

Lys Val Gln Leu Cys Met Leu Tyr Phe Ile Phe Ser Leu Lys Leu Glu
    130                 135                 140

Thr Pro Tyr Thr Ser Ser Asn Lys Lys Ala Gln Gln Ala Leu Gly Phe
145                 150                 155                 160

Ser Leu Ser Leu Leu Gly Pro Cys Thr Tyr Val Arg Phe Tyr Tyr Leu
                165                 170                 175

Phe Gly Gly Val Asn Phe Thr Ala Phe Leu Ala Phe Met His Leu Glu
            180                 185                 190
```

<210> 168
<211> 159
<212> PRT
<213> Homo sapiens

<400> 168

```
Leu Gln Ser Gly Lys Asn Asn Ile Gly Ser Lys Gly Ala Thr Lys Ile
1               5                   10                  15

Pro Gln Cys Leu Glu Arg Arg Lys Val Ser His Leu Ser Ser Asp Ser
            20                  25                  30

Cys Gln Gly Ile Pro Leu Thr Gly Leu Arg Glu Ser Thr Gln Tyr Ala
        35                  40                  45

Phe Leu Ser Ala Glu Asp Ser Asn Thr Ser Lys Ile Ile Leu Ile Phe
    50                  55                  60

Leu Phe Ala Lys Val Tyr Leu Gln Lys Leu Phe Leu Gln Lys Leu Lys
65                  70                  75                  80

Ser Arg Ser Gln Leu Ser Ile Phe Ile Val Leu Thr Ser Arg Leu Thr
                85                  90                  95

Asn Gln Leu Leu Thr Pro Phe Pro Glu Lys Cys Phe Ala Leu Thr Lys
            100                 105                 110

Val Glu Ile Leu Arg Leu Ile Cys Ser Ile Ser Trp Ile His Tyr Ile
        115                 120                 125

Tyr Tyr Leu Ile Tyr Cys Ser Leu Val Val Cys Ile Cys His Tyr Ser
    130                 135                 140

Glu Ile Gln Lys Lys Cys Ser Asn Leu Tyr Leu Tyr Lys Met Tyr
145                 150                 155
```

<210> 169
<211> 173
<212> PRT
<213> Homo sapiens

<400> 169

```
Arg Pro Pro Cys Leu Ser Glu Thr Ala Lys Met Val Ala Tyr Leu Ser
1               5                   10                  15
```

Leu Trp Pro His Pro Arg Glu Val Gly Asn Cys Cys Pro Glu Asn Thr
20 25 30

Gly Gly Gly Gly His Arg Leu Trp Ser Gly Asn Ser Ala Trp Gly Arg
35 40 45

Glu Leu Gly Pro Arg Thr His Val Lys Met Gln Ser Gly Cys Leu Ser
50 55 60

Ile Glu Gln Leu His Cys Ser Gly Gly Leu Phe Gln Ser Leu Val Thr
65 70 75 80

Ser Glu Ser Leu Glu Leu Lys Gly Asn Asn Gly Gly Cys Val Thr Ala
85 90 95

Lys Met Val Ala His Pro Ser His Arg Asp Leu His Pro Arg Glu Ala
100 105 110

Gly Asn His Cys Asn Pro Glu Asn Thr Gly Gly Asp Trp Arg Ala Gln
115 120 125

Ser Thr Val His Ala Glu Leu His Gly Ile Leu Ala Glu Gln Pro Leu
130 135 140

Ile Trp Ser Pro Gly Gln Phe Arg Tyr Leu Gly Phe Pro Ala Lys Val
145 150 155 160

Ala Ala Ile Ala Arg Leu Gly Val Arg Ser Pro Val His
165 170

<210> 170
<211> 228
<212> PRT
<213> Homo sapiens

<400> 170

Phe Pro Leu Gln Tyr His Val Leu Ser Glu His Pro Leu Leu Leu Lys
1 5 10 15

Ser His His Asp Leu Ile Val Trp Asp Ile Phe Gly Leu Ala Leu Phe
20 25 30

Cys Ser Phe Val Thr Phe His Thr Val Leu Ser Lys Thr His Gln Ser
35 40 45

Ser Ser Leu His Trp Leu His Gly Cys Trp Ser Leu Cys Gly Leu Trp
50 55 60

Gln Thr Thr Leu Ser Ile Pro Pro Leu Pro Gly Gln Asn Ser Asp Phe
65 70 75 80

Val Arg Asp Ser Arg Val Pro Gly Lys Leu Asp Phe Leu Gly Ser Phe
85 90 95

Gly Val Lys Val Ala Lys Lys Leu Ser Pro Gly Gln Cys Phe Val Ser
100 105 110

Arg His Leu Trp Ala Gly Leu Leu Glu Thr Leu Leu Phe Phe Trp Ser
115 120 125

Gly Arg Val Leu Phe Ile Pro His Val Ser Leu Phe Trp Phe Gly Lys
130 135 140

Arg Thr Thr Leu Ala Ala Phe Gln Lys Ala Glu Gly Ala Leu Ile Leu

145 150 155 160

Lys Ser Leu Gln Thr Cys Cys Ser Met Gly Arg Thr Asp Leu Tyr Trp
165 170 175

Val Lys Pro Leu Trp Leu Ala Val Leu His Ala Ala Lys Tyr Asp Tyr
180 185 190

Tyr Val Arg Cys Phe Ser Glu Leu Ile Leu Ile Ala Lys Gln Phe Lys
195 200 205

His Val Trp Gly Leu Asn Gly Ile Arg Ala Gly His Gly Gly Ser Arg
210 215 220

Leu Ser Gln His
225

<210> 171
<211> 192
<212> PRT
<213> Homo sapiens

<400> 171

Leu Leu Ala Phe Ser Ile Asn Thr Glu Gly Ser Ile Arg Lys Tyr Ala
1 5 10 15

Leu Leu Trp Met Glu Ser Val Gln Cys Arg Leu Met Gly Phe Leu Ala
20 25 30

Met Leu Ser Thr Glu Val Ser Val Leu Leu Leu Thr Tyr Leu Thr Leu
35 40 45

Glu Lys Phe Leu Val Ile Val Phe Pro Phe Ser Asn Ile Arg Pro Gly
50 55 60

Lys Arg Gln Thr Ser Val Ile Leu Ile Cys Ile Trp Met Ala Gly Phe
65 70 75 80

Leu Ile Ala Val Ile Pro Phe Trp Asn Lys Asp Tyr Phe Gly Asn Phe
85 90 95

Tyr Gly Lys Asn Gly Val Cys Phe Pro Leu Tyr Tyr Asp Gln Thr Glu
100 105 110

Asp Ile Gly Ser Lys Gly Tyr Ser Leu Gly Ile Phe Leu Gly Lys Leu
115 120 125

Tyr Phe Phe Ile Ser Trp Lys Asn Ile Ile Leu Leu Glu Ile Arg Ile
130 135 140

Ser Ala Lys Val Asp Leu Phe Val Ser Glu Ser Glu Ile Thr Ser Arg
145 150 155 160

Leu Cys Pro Phe Ser His Lys Lys Val Phe Thr Ile Val Phe Ile Glu
165 170 175

Val Leu Leu Asn Phe Leu Leu Asp Asn Ile Cys Gly Lys Arg His Thr
180 185 190

<210> 172
<211> 147
<212> PRT
<213> Homo sapiens

<400> 172

Cys Phe Ile Gly Cys Phe Ile Gly Leu Gln Arg Ile Phe Lys Arg Ile
1 5 10 15

Phe Gln Thr Arg Ile Phe Gln Asn Phe Ile Ser Leu Ile His Pro Leu
20 25 30

Phe Ile Tyr Phe Tyr Leu Cys Phe Gln Phe Pro Leu Ile Asp Arg Lys
35 40 45

Phe Thr Cys Ser Lys Met His Arg Thr Ser Val Tyr Asn Ser Ile Ile
50 55 60

Leu Asp Lys Tyr Val His Leu Gly Asn His Leu Asn Gln Asp Thr Glu
65 70 75 80

His Ser Gln His Ser Gly Lys Ile Leu Cys Val His Phe Ser Tyr Ala
85 90 95

Tyr Ser Tyr His Gln Pro Cys Phe Trp Phe Leu Leu Pro Tyr Ile Ser
100 105 110

Leu Ser Cys Pro Ile Ser Arg Lys Trp Asn His Thr Leu Cys Ser Leu
115 120 125

Leu Cys Leu Leu Glu Leu Asn Val Thr Phe Asp Ala Phe Tyr Ile Thr
130 135 140

Gly Cys Thr
145

<210> 173
<211> 197
<212> PRT
<213> Homo sapiens

<400> 173

Cys Ser Ser Ala Leu Met Asp Tyr Pro Phe Leu Val Lys Ile Thr Leu
1 5 10 15

Ile Asn Asn His Tyr Ser Gly Asn Tyr Leu Asn Thr Phe Ala Ser Val
20 25 30

Pro Arg Lys Asn Asn Tyr Phe Gln Asn Lys Lys Val Ala Lys Pro Pro
35 40 45

Pro Asn Pro Thr Lys Ile Ile Arg Ile Pro Arg Met Gly Leu Ile Ile
50 55 60

Ser Leu His Thr Asn Ser Ala Leu Ser Phe Ile Phe Lys Ser Val Arg
65 70 75 80

Glu Asn Ala Ala Ser Cys Leu Thr Phe Phe Val Cys Leu Thr Lys Lys
85 90 95

Leu Thr Ser Ile Val Lys Val Ile Leu Ile Trp Ser Leu Ser Leu Ser
100 105 110

His Tyr Val Gly Phe Asn Phe Leu Ser Gln Glu Asp Thr Ser Cys Ile
115 120 125

Leu Asp Leu Ser Ile Tyr Glu Gln Met Phe Tyr Phe Leu Ser Phe Lys
130 135 140

```
Asn Phe Leu Cys Trp Ile Asn Tyr Lys Thr Gln Thr Phe Leu Lys Gly
145                 150                 155                 160

Lys Tyr Leu Gly Phe Val Asn Ile Asn Phe Glu Asn Val Phe Phe Leu
                165                 170                 175

Ile Leu Leu Ile Leu Thr Leu His Pro Lys Tyr Leu Leu Tyr Phe Leu
            180                 185                 190

Gly Asp Ile Gln Val
        195
```

<210> 174
<211> 168
<212> PRT
<213> Homo sapiens

<400> 174

```
Leu Leu Lys Arg Leu Leu Thr Leu Ser Ser Ser Phe Leu Asn Gln Lys
1               5                   10                  15

Ile Ser Tyr Cys Phe Tyr Leu Leu Arg Val Ser Leu Tyr Phe Ser Phe
            20                  25                  30

Gln Phe Met Leu Ile Ser Lys Leu Pro Cys Ile Ser Lys Gly Leu Ser
        35                  40                  45

Ile Tyr Thr Ile Lys Pro Leu Tyr Val Ser Lys Val Phe Ile Gly Asn
    50                  55                  60

Leu Gly Leu Tyr Asp Pro Lys Leu Cys Trp Ser Thr Thr Phe Ser Val
65                  70                  75                  80

Lys Tyr Leu Ala Ile Lys Tyr Arg Lys Lys Lys Ser Val Gly Gln Arg
                85                  90                  95

Glu Val Met Ile Val Tyr Leu Cys Asn Leu Ile Lys Asn Val Ser Leu
            100                 105                 110

Asn Leu Gln Ser Ile Val Thr Tyr Arg Gly Arg His Tyr Gly Gly Arg
        115                 120                 125

Gly Gly Arg Tyr Lys Val Glu Asn Phe Ser Arg Ala Ser Gln Ser Asn
    130                 135                 140

Lys Ile Gly Ile Tyr Lys Tyr Leu Leu Arg Arg Thr Leu Leu Ser Ala
145                 150                 155                 160

Lys Ile Val Ala Gln Arg Ala Ile
                165
```

<210> 175
<211> 164
<212> PRT
<213> Homo sapiens

<400> 175

```
Gly Gly Gly Gln Glu Ser Tyr Tyr Thr Ile Ile Glu Cys Ser Lys Ser
1               5                   10                  15

Asp Leu Ala His Ser His Met Asn Asp Leu Leu Leu Ile Thr Lys Phe
            20                  25                  30
```

```
Cys Val Leu Ile His Lys Gln Arg Asn Leu Thr Ile Asn Lys Arg Ile
        35                  40                  45

His Tyr Pro Ala Asn Val Ile Leu Cys Thr Val Gln Ser Ile Thr Asp
    50                  55                  60

Leu Asn Glu Pro Tyr Val Val Glu Cys Leu Ile Met His Phe Ser Ile
65                  70                  75                  80

Val Tyr Gly Leu Asn Lys Leu His Ile Thr Tyr Lys Ser His Trp Leu
                85                  90                  95

Leu Tyr Thr Leu Val Asn Cys Lys Pro Lys His Ser Arg Leu Gly Asn
            100                 105                 110

Lys Tyr Thr Phe Leu His Lys Asn Ser Ile Ala Ser Gly Ala Val Leu
        115                 120                 125

Pro Val Trp Phe Thr Leu His Pro Asp Thr Ser Asn Tyr Thr Val Leu
    130                 135                 140

Asn Glu Ser Leu Cys Ser His Ile Asn Lys Leu Ser Pro Phe Asn Phe
145                 150                 155                 160

Ser Tyr Asn Lys


<210>  176
<211>  186
<212>  PRT
<213>  Homo sapiens

<400>  176

Thr Ala Leu Leu Tyr His Arg Asp Met Pro Gly Asn Ser Ser His Gln
1               5                   10                  15

Met Leu Ser Gly Gly Val Pro Met Arg Lys Arg Pro Gln Val Ser Gln
            20                  25                  30

Thr Ala Gln Arg Tyr His Asp Asp Gly Arg Leu Phe Pro Trp Cys Leu
        35                  40                  45

Gly Arg Leu Leu Ser Phe Ile Thr His Leu Phe Arg Arg Glu Val Thr
    50                  55                  60

Met Gln Arg Gly Cys Leu Val Leu Leu Pro Gly Cys Lys Pro Trp Gly
65                  70                  75                  80

Pro His Ser His Pro Trp Glu Gln Arg Met Trp Glu Gln Asn Phe Arg
                85                  90                  95

Cys Ser Asn Ser Lys Gly Ala Trp Pro Leu Ser Val Ser Leu Pro Glu
            100                 105                 110

Ser Arg Ala Gln Ala Lys Thr Gln Ala Pro Ser Arg Pro Leu Trp Gln
        115                 120                 125

Val Thr Thr Ser Leu Pro Thr Thr Ile Thr Ser Pro Pro Tyr Gln Gln
    130                 135                 140

Ile Leu Asp Ser Leu Gln Leu Pro Ile Lys Gly Lys Pro Pro Lys Ala
145                 150                 155                 160
```

```
Lys Pro Asp Phe Pro Ile Leu Lys Cys Leu Asn Arg Glu Gly His Ser
                165                 170                 175

Gly Phe Met Ser Ile Ile Pro Ala Phe Glu
            180                 185
```

<210> 177
<211> 217
<212> PRT
<213> Homo sapiens

<400> 177

```
Ala Ala Phe Ser Ala Leu Pro Arg Val Leu Cys Gly Pro Pro Glu Val
1               5                   10                  15

Gln Leu Val Ser His Gly Leu Val Phe Phe Thr Ala Met Leu Phe Asp
            20                  25                  30

Ala Ile Lys Thr Ser His Cys Gln Ser Ala Cys Phe Leu Leu Gly Ala
        35                  40                  45

Ser Phe Leu Thr Arg Arg Ser Gln Lys Pro Arg Pro Gly Gly Asp Leu
    50                  55                  60

Ser Arg Leu Thr Ser Gly Val Gly Thr Leu Cys Pro Ser Ser Val Phe
65                  70                  75                  80

Leu Glu His Pro Gly Glu Pro Ala Ala Arg Arg Ser Pro Thr Ala Gly
                85                  90                  95

His Val Glu Ala Asn Ser Pro Pro Thr Gln Thr Ala Trp Ala Met Leu
            100                 105                 110

Lys Arg Ala Ser Ala Pro Asn Asp Phe Ser Glu Val Gln Thr Ser Pro
        115                 120                 125

Arg Leu Ser Ala Ser Glu Ser Leu Pro Leu Gln Pro Arg Pro Leu His
    130                 135                 140

Gly Gly Arg Gly Gly Asp Thr Gln Lys Phe Gly Phe Phe Gly Ala Ala
145                 150                 155                 160

His Thr Gln Asp Val Ser Gly Ala Gly Lys Gly Ser Lys Trp Ser Leu
                165                 170                 175

Cys Arg Asn Thr Cys Ala Arg Leu His Gly Phe Thr Thr Thr Arg Arg
            180                 185                 190

Gln Leu Lys Ile Pro Thr Thr Pro Gly Val Ser Trp Leu Val Ser Arg
        195                 200                 205

Ser Leu Thr His Gly Thr Ala Leu Thr
    210                 215
```

<210> 178
<211> 187
<212> PRT
<213> Homo sapiens

<400> 178

```
Lys Tyr Asn Tyr Ile Ser Ile Tyr Met Tyr Ser Leu Arg Asn Asn Lys
1               5                   10                  15
```

Met Asn Ile His Val Phe Ser Leu Pro Ser Phe Phe Phe Leu Ile Pro
20 25 30

Cys Ile Gln Phe Glu Ala Phe Lys Asn Phe Ile Phe Leu His Leu Tyr
35 40 45

Leu Met Leu Leu Ala Thr Leu Gly Tyr Phe Leu Ser Pro Ile Leu Ile
50 55 60

Phe Gly Cys Ser Tyr Ile Ser Ile Ile Lys Arg Glu Ser Asp Val Gly
65 70 75 80

His Ser Tyr Ser Val Val Cys Asn Leu Asn Tyr Ser Glu Ile Ser Arg
85 90 95

Val Leu Ser Leu Pro Ser Met Leu Gln Val His Cys Cys Gly Ser Asn
100 105 110

Met Asp His Phe Cys Ser Phe Cys Ile Ser Ile Tyr Asp Asn Gln Tyr
115 120 125

Leu Ser Ile Leu Ile Gln Ile His Lys Tyr Phe Ser Gly Pro Leu Asn
130 135 140

Leu Lys Ile Cys Leu Leu Lys Thr Leu Ile Ser Phe Glu Tyr Asp Cys
145 150 155 160

Pro Thr Phe Leu Phe Gly Phe Leu Leu Gly Lys Phe Val Leu Asp Arg
165 170 175

Cys Trp Glu Leu Trp Asp Ile Cys Leu His Val
180 185

<210> 179
<211> 115
<212> PRT
<213> Homo sapiens

<400> 179

Leu Ile His Thr Leu Cys Ala Ile Val Cys Asn Ser Asn Thr Gln Arg
1 5 10 15

Cys Lys Phe Glu Ser Phe Ser Thr Leu Ala Ala Tyr Trp Asn Tyr Pro
20 25 30

Gly Val Phe Thr Ile Ser Asp Ile Gln Val Ile Val Leu His Ser Lys
35 40 45

Thr Glu Asn Ser Ala Phe Asp Leu Tyr Glu Cys Leu Pro Pro Val Leu
50 55 60

Ser Phe Phe Tyr Pro Leu Gln Gln Thr Thr Lys Leu Ser Ile Phe Ile
65 70 75 80

Leu Leu Ala Gly Phe Lys Leu Gln Ala Ile Val Trp Leu Arg Lys Phe
85 90 95

Asn Tyr Tyr Thr Phe Ile Glu Cys Thr Leu Ile Cys Gln Glu Ile Gly
100 105 110

Gln Ile Lys
115

<210> 180

<211> 196
<212> PRT
<213> Homo sapiens

<400> 180

Leu Leu Met Gln Leu Pro Lys Thr Leu Phe Lys Ile Val Ser Asn Lys
1 5 10 15

His Glu Cys Ser Glu Asn Ser Leu Glu Thr Leu Ile Arg Lys Trp Pro
20 25 30

His Ser Arg His His Cys Gly Ile Ser Thr Lys Trp Asp Ser Gly Asp
35 40 45

Glu Glu Phe Ser His Glu Arg Arg Gln Leu Pro Asn Glu Val Glu Arg
50 55 60

Lys Asp Val Glu Ser Leu Gln Asn Asn Ser Pro Leu Ser Leu Met Lys
65 70 75 80

Gly Lys Asn Ser Gln Asn Ser Thr Ala Glu His Glu Thr Asn Leu Asn
85 90 95

Tyr Phe Arg Ala Met Asn Lys Ile Asn Ser Ile Thr Phe Ile Leu Cys
100 105 110

Pro Gln Phe Phe Gln Val Asn Tyr Leu Leu Ala Phe Asp Tyr Tyr Phe
115 120 125

Val Ser His Lys Ile Cys Tyr Glu Ser Met Tyr Arg Ile Leu Ser Asp
130 135 140

Trp Leu Cys Tyr Cys Asn Gln Arg Cys Val Asp His Pro Val Gln Cys
145 150 155 160

Trp Gln Asp Ile Pro Tyr Ile Met Asn Phe His Ser Pro Leu Leu Ala
165 170 175

Val Cys Gly Leu Thr Asn Lys Tyr Ser Ile Leu Ile Leu Gln Ala Ile
180 185 190

Arg His Phe Ala
195

<210> 181
<211> 216
<212> PRT
<213> Homo sapiens

<400> 181

Lys Trp Asp Ser Ile Phe Arg Asn Val Cys Ile Leu Tyr Asp Phe Gly
1 5 10 15

Asn Leu Arg Lys Tyr Gly Arg Lys Lys Asn Leu Ile Leu Phe Ser Asp
20 25 30

Asn Cys Gly Tyr Ser Phe Lys Pro His Lys Ser Leu Thr Asn Arg Ile
35 40 45

Phe Ser Lys Val Ser Tyr Asn Val Glu Ser Val Thr Val Leu Met Thr
50 55 60

Phe Phe Val Leu Cys Tyr Ile Lys Ile Ser Ser Val Leu His Leu Asp

65 70 75 80

Arg Asn Phe Phe Ala Ser Phe Cys Thr Ser Leu His Glu Leu Phe Gly
85 90 95

Asn Tyr Leu Thr Asp Leu Cys Ser Tyr Lys Cys His Val Ser Leu Tyr
100 105 110

Asn Ile Lys Ile Ala Phe Val Asn Ile Ile Ile Thr Leu Ala Ser Lys
115 120 125

Asp Trp Asp Ala Asn Lys Leu Thr Val Asp Ala Thr Phe Phe Pro Lys
130 135 140

Leu Glu Phe Cys His Trp Gln His Ile Leu Pro Val Ile Phe Leu Glu
145 150 155 160

Val Thr Gly Leu Cys Tyr Phe Leu Lys Arg Met Cys Ala Lys Tyr Pro
165 170 175

Ser Leu Ser Asn His Ser Ser Ser Val Ser Gly Phe Leu Ser Gly Asn
180 185 190

Asp Val Pro Leu Lys Lys Val Ala Asn Ser Ser His Asn Ser Ile Val
195 200 205

Val Leu Phe Leu Glu Val Thr Ile
210 215

<210> 182
<211> 182
<212> PRT
<213> Homo sapiens

<400> 182

Pro Ser Pro Gln Phe Asn Tyr Leu Pro Pro Cys Pro Ser His Asn Thr
1 5 10 15

Trp Glu Phe Lys Val Arg Ser Glu Trp Gly Gln Ser Glu Thr Ile Leu
20 25 30

Ile Ile Ser Asp Cys Lys Leu Tyr Glu Ala Lys Lys Tyr Val Phe Cys
35 40 45

Ser Pro Leu Tyr Leu Lys His Leu Ala Tyr Leu Ala Asn Arg Cys Leu
50 55 60

Met Asn Tyr Leu Phe Asn Gly Cys Ser Phe Val Leu Val Thr Leu Gln
65 70 75 80

Gly His Phe Phe Pro Cys Gly His Gly Gln Thr Val Leu Trp Leu Val
85 90 95

Ala Val Met Met His Gly Ser Thr Gly Val Leu Pro Thr Gly Leu Leu
100 105 110

Lys Thr Ile Asn Asn Phe Ser Ile Ser Ala Asn Arg Asn Leu Ile Tyr
115 120 125

Phe Cys Leu Trp Leu Cys Phe Leu Phe Phe Arg Ala Gln Ser Pro Ile
130 135 140

Cys Leu Lys Leu Phe Phe Phe Ser Phe Ala His Ile Leu Asn Gln Phe
145 150 155 160

Leu Val Tyr Gln Ile Ser Thr Glu Asp Cys Thr Gln Asp Gly Arg Pro
165 170 175

Lys His Thr Cys Ser Thr
180

<210> 183
<211> 196
<212> PRT
<213> Homo sapiens

<400> 183

His Thr Tyr Leu Tyr Phe Pro Pro Ala Val Thr Leu Lys Phe Ser Gln
1 5 10 15

Leu Arg Gln Gln Ile Asp Phe Ile Ser Leu Ser Pro Leu Gln His Gln
20 25 30

Ile Lys Ala Phe Phe Leu Gly Thr Thr Leu Cys Leu Ser Asp Trp Leu
35 40 45

Ser Val Leu Arg Ala Thr Val Pro Arg Pro Asn Pro Trp Pro Ser Ser
50 55 60

Thr Gln Glu His Ser Gly Lys Gly Met Pro Phe Asn Phe Gln Ala Cys
65 70 75 80

Thr Asn Pro Gly Leu Trp Thr Arg Arg Arg Tyr Leu Trp Met Asn Arg
85 90 95

Gly Ser Ser Lys His Phe Ser Cys Arg Phe Tyr Ser Asn Pro Glu His
100 105 110

Ile Leu Cys Val Ala His Arg Ile Phe Phe Leu Phe Asn Ser Val Asp
115 120 125

Leu Met Ile Thr Arg Phe Ser Ala Val Asp Cys Gly Pro Tyr Pro Leu
130 135 140

Cys Leu His Ile Tyr Phe Ser Lys Trp Lys Asp Val Ser Arg Thr Val
145 150 155 160

Lys Lys Ile Ile Phe Thr Leu Asn Ile Leu Phe Leu Pro Asp Thr Ser
165 170 175

Phe Ser Ile Val Leu Leu Thr Ile Leu Lys Ser Asn Gln Asn Leu Asn
180 185 190

Phe Gln Tyr Ile
195

<210> 184
<211> 139
<212> PRT
<213> Homo sapiens

<400> 184

Leu Leu Ala Ile Asn Phe Trp Gly Glu Lys Gly Gln Asn Arg Asn Arg
1 5 10 15

Ala Thr Gln Glu Val Lys Phe Lys Trp Ile Asn Trp Ser Leu Leu Asn
20 25 30

```
Gln Gln Ile Cys Cys Lys Gln Asn Arg His Ser Met Met Pro Cys Ile
        35                  40                  45

Val Leu Phe Asn Ile Thr Leu Leu Ile Ser Arg Val Cys Val Cys Val
    50                  55                  60

Cys Val Cys Val Ser Cys Val Leu Thr Tyr Tyr Gly Ser Thr Ser His
65                  70                  75                  80

Ala Thr Ser Leu Ala Leu Leu Leu Ser Arg Glu Cys Arg Gly Leu Leu
                85                  90                  95

Val Leu Ser Ala Met Phe Asn Ser Ala Ser Thr Met Ile Gly Phe Gln
            100                 105                 110

Ile Gln Lys Asn Ala Phe Leu Cys Ile Arg Asn Pro Asn His His Lys
        115                 120                 125

Asn Ile Gln Lys Arg Met Asn Ile Phe Leu Leu
    130                 135
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<210> 185
<211> 204
<212> PRT
<213> Homo sapiens

<400> 185

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Phe Pro Ser Leu Gly Ile Tyr Cys Glu Val Leu Leu Val Thr Phe Ser
1               5                   10                  15

Lys Val Ile Gly Thr Ser Pro Ala Thr Ile Ser Ser Phe Ser Phe His
            20                  25                  30

Val Cys Leu Cys Ser Phe Leu Ser Cys Gln Lys His Leu Lys Cys Ile
        35                  40                  45

Ile Phe Thr Leu Cys Cys Phe Cys Tyr Cys Lys Ser Asn Phe Lys Val
    50                  55                  60

Ile Cys Thr Pro Val Leu Phe Leu Gln Lys Tyr Phe Leu Val Leu Asn
65                  70                  75                  80

Asp His Asn Lys Arg Val Gly Gly Asp Phe Thr Thr Gly Lys Ile Thr
                85                  90                  95

Gln His Glu Lys Ala Ala Phe Val Asn Leu Ser Phe Asn Arg Ala Ala
            100                 105                 110

Pro Val Ile Leu Thr Glu Thr Lys Val Lys Tyr His Cys Val Thr Arg
        115                 120                 125

Leu Phe Val Thr Asn Met Ser Ile Asn Ile Asn Ala Met Ala Ala Leu
    130                 135                 140

His Ser Gly Gly Gly Val Trp Cys Trp Val Ala Ala Gln Ile Thr Tyr
145                 150                 155                 160

Ile Asn Asn Ser Gln Ser Gln Leu Cys Asn Ile Ile Lys Ala Leu Leu
                165                 170                 175

Lys Tyr Val Ser Val Pro Glu His His Pro Ser Glu Ile Leu Ile Gln
            180                 185                 190
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Leu Ile Leu Pro Val Lys Glu Ser Ile His Thr Phe
195 200

<210> 186
<211> 170
<212> PRT
<213> Homo sapiens

<400> 186

Cys Leu Asn Val Leu Arg Lys Leu Cys Ala Gln Lys Gln Thr Tyr Ser
1 5 10 15

Gly Leu Met Val Cys Ser Thr His Thr His Thr Lys Trp Pro Phe Ser
20 25 30

Gln Ser Ser Trp Leu Ser Ser Thr Ser Pro Cys His Thr Cys Ile Gln
35 40 45

Ile Thr Leu Ser Val Ile His Cys Arg Asn Leu Ile Asn Lys Lys Ser
50 55 60

Leu Val Ile Thr Gly Pro Ser Leu Ala Phe Phe Tyr Trp Pro Asn Ala
65 70 75 80

Glu Tyr Phe Trp Leu Glu Met Ile Thr Leu Phe Ala Glu Ser Arg Leu
85 90 95

Ala Leu Gly Leu Met Ile Leu Ser Ser Cys His Ser Leu Phe His Ile
100 105 110

His Trp Arg Arg Leu Phe Pro Gly Glu Gly Ala His Asn Cys Ala Cys
115 120 125

Leu Phe Gln Asp Val Ser Leu Gly Thr Met Leu Gly Ser Asp Phe Pro
130 135 140

Arg Val Arg Ser Ala Leu Cys Leu Ala Phe Trp Leu His Pro Cys Ala
145 150 155 160

Gln Arg Arg Asp Arg Val Lys Glu Leu Arg
165 170

<210> 187
<211> 216
<212> PRT
<213> Homo sapiens

<400> 187

Leu Leu Thr Lys Pro Ser Phe Asn Val Asn Ala Leu His Cys Ile Ile
1 5 10 15

His Tyr Ile Ile Asn Asn Pro Cys Val Cys Val Cys Val Cys Val Cys
20 25 30

Val Cys Val Leu Thr Tyr Tyr Gly Ser Thr Ser His Ala Thr Ser Leu
35 40 45

Ala Leu Leu Leu Ser Arg Glu Cys Arg Gly Leu Leu Val Leu Ser Ala
50 55 60

Met Phe Asn Ser Ala Ser Thr Met Ile Gly Phe Gln Ile Gln Lys Asn
65 70 75 80

Ala Phe Leu Cys Ile Arg Asn Pro Asn His His Lys Asn Ile Gln Lys
85 90 95

Arg Met Asn Ile Phe Leu Leu His Phe Phe Val Val His Tyr Leu Asp
100 105 110

Phe Ile Ile Ile Ile Leu Arg Lys His Leu Glu Lys Leu Gly Asn Val
115 120 125

Ala Ala Leu Phe Ile Lys Glu Gly Lys Gly Glu Thr Arg His Leu Lys
130 135 140

Ser Lys Ile Arg Asn Asp Phe Arg Thr Asn Ile Phe Asn Asn Leu Ser
145 150 155 160

Val Arg Glu Lys Phe Trp Tyr Phe Leu Lys Thr Ile Cys Leu Cys Ile
165 170 175

Arg Pro Phe His Leu Asp Tyr Arg Gln Ile Met Cys Lys Phe Ile Ser
180 185 190

Val Lys Thr Val Lys Asp Arg Leu Leu Pro Glu Pro Leu Asn Ile Phe
195 200 205

Leu Ser Lys Phe Arg Asp His Phe
210 215

<210> 188
<211> 146
<212> PRT
<213> Homo sapiens

<400> 188

Cys Gly His Cys Gly Ala Gly Ser Leu Gly Phe Ser His Ser Thr Gln
1 5 10 15

Gln Val Val Ser Val Val Asp Asn Tyr Glu Val Phe Tyr Met His Arg
20 25 30

Ile Ile Leu Asp Thr Leu Gly Lys Leu Tyr Lys Lys Asn Arg Phe Tyr
35 40 45

Phe Val Ser Tyr Thr Asp Asp Ile Ile Lys Thr Lys Thr Thr Asn Leu
50 55 60

Ala Arg Gly Gly Asp Asn Glu Asn Leu Ser Leu Leu Tyr Gln His Leu
65 70 75 80

Gln Ala Tyr Phe Val Tyr Leu His Phe Ala Leu Leu Cys Phe Ile Asp
85 90 95

Ile Ala Tyr Phe Thr Asn Arg Thr Thr Ala Thr Leu His Arg Ala Ser
100 105 110

Phe Leu Glu Pro Phe Leu Gln His His Val Leu Thr Ser Cys Leu Cys
115 120 125

Tyr Phe Leu Gln Tyr Phe Pro Phe Tyr Tyr Tyr Cys Val Cys Asp Asn
130 135 140

Leu Ser
145

<210> 189

<211> 206
<212> PRT
<213> Homo sapiens

<400> 189

Leu Gly Leu Gln Ala Ala Thr Ala Thr Gly Leu His His Cys Phe Lys
1 5 10 15

Ser Phe Leu Ser Ile Val Pro Arg Cys Ile Leu Asp Asn Phe Gln Glu
20 25 30

Gly Asp Leu Leu Asp Ser His Lys Arg Phe Val Leu Cys Trp Gln Leu
35 40 45

Ser Ile Lys Ser Leu Ala Lys Pro Pro Leu Tyr Thr Ala Thr Val Gly
50 55 60

Thr Ile Val Asn Tyr Cys Leu Pro Gly Ile Met Ile Arg Gln Pro Tyr
65 70 75 80

Ile Tyr Phe Cys Ile Phe Asn Leu Tyr Ile Leu Arg Ile Ser Asp Tyr
85 90 95

Ile Gly Tyr Tyr Thr Val Cys Ile Cys Thr Asn His Leu Ile Ser Phe
100 105 110

Lys Val Ile Val Leu Gly Ile Lys Met Asn Cys Ser Asn Ile Tyr Ile
115 120 125

Phe Lys Cys Thr Glu Ser Arg Tyr Thr Glu Leu Phe Arg Ile Phe Phe
130 135 140

Leu Leu Gly Ile Ala Leu Ser Ile Phe Thr Ile Pro Val Ile Cys Ile
145 150 155 160

Leu Tyr Tyr Phe Val Ser Asn Asn His Ile Leu Phe Asp Asp Met Val
165 170 175

Met Leu Phe Phe Ile Val Lys Trp Trp Ser Pro Gly Arg Ala Gln Trp
180 185 190

Leu Thr Pro Pro Asn Pro Gln His Phe Gly Arg Pro Arg Arg
195 200 205

<210> 190
<211> 212
<212> PRT
<213> Homo sapiens

<400> 190

Ile Ser Pro Glu Pro Thr Lys Arg Asp Lys His Ser Val Val Phe Phe
1 5 10 15

Ser Ala Leu Ile Gln Leu Cys Cys Lys Phe Leu Phe Ser Glu Glu Thr
20 25 30

Pro Arg Ser Met Thr Glu Ile Phe Phe Pro Phe Pro Phe Cys Asp Val
35 40 45

His Leu Ser Ile Leu Asp Ala Cys Thr Pro Glu Leu Thr Ser His Ser
50 55 60

Glu His Ala Gln His His Thr Leu Pro Ser Ser Pro Ala Arg Thr Val

65 70 75 80

His Ser Ser Ser Cys Val Asn Pro Trp Leu Ser Phe Leu Phe Arg Thr
85 90 95

Ala Phe Gln Ala Pro Trp Thr Leu Thr Leu Thr Ser Tyr Ala Gln Lys
100 105 110

Arg Leu Trp Glu Thr Glu Val Thr Ile Ser Gly Phe Arg Met Ala Phe
115 120 125

Phe Cys Ser Arg Lys Glu Pro Ala Val Pro Gln Val Leu Phe Leu Val
130 135 140

Pro Tyr Ser Ser Ala Pro Leu Arg Ile Lys Glu Val Gly Thr Val Ser
145 150 155 160

Ser Leu Tyr Ser Tyr Ile Ile Glu Ser Asn Tyr Phe Cys Asn Leu Leu
165 170 175

Ser Ser Ser Gly Tyr Tyr Met Asn Glu His Ser Val Pro Phe Ile Asp
180 185 190

Leu Leu Ser Gly Tyr Ile Leu Ala Phe Asn Ile Leu Tyr Leu Leu His
195 200 205

Tyr Leu Gly Leu
210

<210> 191
<211> 201
<212> PRT
<213> Homo sapiens

<400> 191

Leu Leu Ser Pro Gln Pro Pro Lys Glu Leu Arg Leu Pro Thr Asn Val
1 5 10 15

Pro Ser Ile Phe Lys Thr Leu Ser Trp Tyr Thr Asp His Asn Asn Ser
20 25 30

Tyr Ile Ile Val Asn Leu Ser Pro Phe Ile Cys Asn Ser Pro Gly Phe
35 40 45

Pro Cys Ser Phe Tyr Met Ser Lys Ala Pro Leu Glu Tyr Ile Thr Phe
50 55 60

Ser Ser Cys Ile Phe Gly Ser Tyr Leu Gln Phe Leu Thr Leu Pro Leu
65 70 75 80

Phe Leu Lys Thr Leu Thr Phe Leu Arg Ile Thr Gly Gln Val Phe Tyr
85 90 95

Arg Met Ala Phe Ser Trp Tyr Phe Cys Leu Met Val Phe Ser Leu Ala
100 105 110

Trp Gly Lys Val Phe Trp Glu Glu Asp Ser Arg Asp Glu Glu Val Leu
115 120 125

Phe Ile Ser Pro Pro Ile Lys Val His Ala Val Asn Ile Thr Asn His
130 135 140

Cys Cys Pro Trp Ser Ala Gly Leu Arg Ser Tyr Leu Ser Gly Cys Phe
145 150 155 160

Thr Met Asn Phe Phe Ser Phe Val Leu Pro Phe Tyr Thr Thr Leu Ser
165 170 175

Gly Lys Thr Ile Thr Met Asp Ser Leu Tyr Leu Arg Asn Gly Asn Tyr
180 185 190

Gly Leu Pro Leu Ile Tyr Arg Leu Phe
195 200

<210> 192
<211> 180
<212> PRT
<213> Homo sapiens

<400> 192

Ser Ala Ser Thr Leu Leu Tyr Cys Thr Pro Leu Asn Pro Cys Gln Thr
1 5 10 15

Gln Gly Ile Ile Asn Ser Gln Ile Ala Pro Ser Ala Ser Ala Phe Lys
20 25 30

Val Gln Tyr Phe Ser Arg Val Ala Asn Lys Leu Thr Thr Cys Pro Lys
35 40 45

Thr Thr Glu Ile Tyr Ser Leu Ile Val Trp Arg Pro Lys Ser Arg Trp
50 55 60

Trp Gln Gly Cys Ile Leu Ser Lys Gly Ser Ile Pro Cys Phe Phe Gln
65 70 75 80

Leu Leu Met Ala Pro His Ile Pro Trp Leu Val Ala Thr Ser Leu Ser
85 90 95

Tyr Leu Pro Trp Trp Ser His Gly Leu Leu Leu Phe Val Leu Phe Ser
100 105 110

Val Ser Phe Phe Tyr Lys Asp Ile Cys His Trp Ile Ser Pro Pro Arg
115 120 125

Lys Phe Arg Ile Ile Leu Pro Asp Ser His Leu Gln Pro Phe Glu Gly
130 135 140

Leu Pro Ser Leu Phe Phe Phe Pro Tyr Lys Ile Thr Phe Thr Gly Ser
145 150 155 160

Gly Asn Leu Asp Met Asp Ile Phe Trp Val Glu Lys Gly Thr Ile Pro
165 170 175

Asn Thr Ala Cys
180

<210> 193
<211> 176
<212> PRT
<213> Homo sapiens

<400> 193

Pro Phe Asn Glu Met Ser Ile Ile Tyr Leu Asn Ile Ser Leu Asp Ser
1 5 10 15

Lys Leu Gln Val Tyr Leu Gln Val Leu Ile Ser Leu His Phe His Asn
20 25 30

Tyr Phe Ile Leu Ile Val Tyr Leu Asp Tyr Leu Arg Asn Leu Gln Leu
35 40 45

Ser Phe Asn Val Thr Phe Leu Ser Thr Ile Leu Leu Val Asp Phe Arg
50 55 60

Cys Leu Pro Val Arg Thr Leu Ser Leu Asp Thr Leu Phe Tyr Lys Ile
65 70 75 80

Ile Gln Val Leu Ala Ile Phe Ile Lys Pro Ile Leu Met Ser Tyr Leu
85 90 95

Ser Lys Ile Thr Gln Ala Lys Val Ile Ser Val Leu Val Trp Val Tyr
100 105 110

Ile Leu Ile Thr Leu Ile Ser Asn Phe Asp Pro Leu Tyr Phe Gly Arg
115 120 125

Asp Thr Tyr Ser Leu Leu Thr Pro Glu Lys Gly Val Leu Gln Arg Asn
130 135 140

Lys Leu Trp Met Ser Thr Lys Leu Gly Arg Leu Lys Ile Leu Arg Lys
145 150 155 160

Arg Gly Ala Pro Lys Leu Gln Gln Phe Val Leu Leu Ile Ala Ile Lys
165 170 175

<210> 194
<211> 88
<212> PRT
<213> Homo sapiens

<400> 194

Ser Tyr Val Phe Cys Gln Pro Ser Leu Asn Cys Gly Lys Leu Ile Cys
1 5 10 15

Leu Ala Asn Ser Val Lys Pro Tyr Thr Leu Tyr Ser Ser Gln Leu Tyr
20 25 30

Phe Gln Gln Gln Asn Asp Leu Met Arg Lys Ala Ala Leu Thr Phe Ser
35 40 45

Cys Lys Ser Pro Met Ser Ser Leu Val Val Glu Ser Val Leu Ala Ser
50 55 60

Asp Thr Phe Tyr Ser Cys Asn Met Leu Phe Trp Leu Lys Tyr Val Thr
65 70 75 80

Lys Ile Trp Ser His Thr Asp Ile
85

<210> 195
<211> 204
<212> PRT
<213> Homo sapiens

<400> 195

Val Ser Ser Ala Leu Thr Cys Ser Leu Pro Gly Pro Ala His Gln Thr
1 5 10 15

Cys Ser Cys Leu Lys Ala Leu Pro Trp Glu Tyr Ser Ser Pro Leu Gln
20 25 30

Ser Trp Val Leu Gln Ser Trp Val Leu Pro Ile Ile Gln Phe Lys Ile
35 40 45

Thr Ser Trp Asp Arg Ser Ser Gln Thr Asn Gln Cys Gly Val Pro Phe
50 55 60

Leu His Arg Arg Cys Ser Thr Ile Thr Ser Leu Cys Cys Ile Leu Leu
65 70 75 80

Thr His Ser Ser Gln Ile Ile Leu Cys Ile His Phe Val Ser Phe Leu
85 90 95

His Leu Pro Arg Ala Thr Leu Ser Val His Val Ala Pro Gly Leu Glu
100 105 110

Cys Tyr Phe His His Ser Thr His Phe Ser Leu Val Asn Cys Asp Ser
115 120 125

Ser Ala His Phe Arg Thr Leu Ser Ser Asp Leu Arg Ile Arg Gly Ile
130 135 140

Asp Thr Arg Val Gly Gly Met Tyr Arg Leu Leu Ile Asp Glu Asn Glu
145 150 155 160

Lys Ile Ala Arg His Cys Ser Thr Val Glu Val Arg His Glu Leu Cys
165 170 175

Ile Phe Gln Asp Phe Leu His Leu Leu Leu Thr Ala Trp Val Arg Ile
180 185 190

Glu Arg Leu Thr Thr Glu Thr Thr Ile Leu Gly Arg
195 200

<210> 196
<211> 190
<212> PRT
<213> Homo sapiens

<400> 196

Cys Cys Leu Asp Glu Val Gly Arg Asp Ser Tyr Leu Met Leu Pro Leu
1 5 10 15

Leu Ser Cys Ser Trp Asn Lys Ser Gln Trp Ser Leu Arg Trp Glu Lys
20 25 30

Leu Asn Asp Ile Cys Ser Leu Cys Ser Cys Gln Pro Cys Pro Leu Glu
35 40 45

Ala Pro Thr Leu Phe Leu Leu Lys Leu Pro Ser Val Gln Ile Leu Arg
50 55 60

Ser Leu Ser Met Ile Ser Phe Pro Ile Ile Val Asp Tyr Cys Leu Asn
65 70 75 80

Leu Gly Thr Ile Phe Gln Cys Met Ile Glu Ser His Leu Gly Lys Ile
85 90 95

Tyr Ser His Trp Tyr Leu Lys Glu Arg His Ser Tyr Ser Gly Ser Leu
100 105 110

Val Tyr Ile Gly Asn Trp Phe Gln Asp Pro Leu Arg Ile Gln Lys Ser
115 120 125

```
Lys His Ile Gln Ala Val Pro Lys Leu Ala Leu Trp Asn Ser Pro Val
    130                 135                 140

Arg Lys Val Gly Leu Pro Tyr Leu Gln Val Leu Tyr Ser Val Ser Thr
145                 150                 155                 160

Leu Leu Leu Ile Cys Ile Trp Leu Lys Lys Ile Cys Val Met Asp Pro
                165                 170                 175

Cys Ser Ser Asn Pro Cys Cys Ser Arg Val Asn Cys Ile Ala
            180                 185                 190

<210>  197
<211>  197
<212>  PRT
<213>  Homo sapiens

<400>  197

Gln His Ser Glu Ile Pro Ser Leu Lys Arg Ile Thr Leu Leu Trp Cys
1               5                   10                  15

Gly His Lys Arg Arg Gln Ile Leu Lys Glu Asp Leu Asn Asn Trp Lys
            20                  25                  30

Val Tyr Ile Leu Phe Pro Ile Met Ser Phe Ser Val Pro Phe Pro Leu
        35                  40                  45

Asp Leu Phe Tyr Phe His Phe Ser Ala Val Ile Leu Tyr Leu Phe Ile
    50                  55                  60

His Cys Glu His Ile Phe Leu Tyr Val Leu Lys Leu Leu Thr Ile Ile
65                  70                  75                  80

Ala Tyr Arg Phe Leu Leu Leu Lys Lys Ile Trp Ile Phe Leu His Trp
                85                  90                  95

Leu Cys Phe Leu Leu Asn Met Gly Ile Phe Leu Val Phe Ser Tyr Val
            100                 105                 110

Glu Phe Ile Ile Phe Thr Met Ile Cys Gly Asp Trp Ile Leu Leu Ser
        115                 120                 125

Leu Asn Val Leu Leu Ile Trp Pro Phe Leu Phe Ser Phe Phe Phe Ser
    130                 135                 140

Phe Leu Ser Lys Glu Leu Ile Leu Ala Glu Phe Trp Ser Pro Leu Pro
145                 150                 155                 160

Ser Pro Pro Leu Ser Ser Phe Leu Phe Leu Ser Phe Leu Ser Lys Gly
                165                 170                 175

Leu Thr Leu Ala Glu Phe Arg Phe Gln Thr Ile Val Ser Phe Val Val
            180                 185                 190

Gly Arg Ser Asn Phe
        195

<210>  198
<211>  210
<212>  PRT
<213>  Homo sapiens

<400>  198
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Phe Phe Ser His Phe Leu Asn Tyr Tyr Phe Pro Leu Phe Leu Val His
1               5                  10                  15

Phe Leu His Ile Leu Ile Thr Phe Leu Phe Pro Phe Val Tyr Ile Leu
            20                  25                  30

Trp Ile Phe Ser Leu Trp Leu Pro Trp Arg Leu His Val Thr Val Gln
        35                  40                  45

Ser Tyr Asn Asn Leu Phe Ile Asn Thr Asn Leu Thr Ser Ile Ala Pro
    50                  55                  60

Asn Thr Leu Leu Phe Tyr Asn Phe Pro Phe Leu Leu Cys Tyr Val Ile
65                  70                  75                  80

Ser Val Lys Asn Gln Ser Leu Tyr Met Leu Cys Thr Tyr His Gly Phe
                85                  90                  95

Ile Ile Ile Phe Val Asn Leu Pro Phe Lys Phe Phe Lys Lys Ser Val
            100                 105                 110

Val Thr Ser Gln Asn Tyr Ile Lys Leu Leu Val Phe Ile Met Ser Met
        115                 120                 125

Tyr Leu Pro Leu Pro Glu Ile Phe Ile Phe Ser Tyr Val Phe Lys Leu
    130                 135                 140

Leu Ser Ile Val Ile Leu Phe Gln Leu Arg Ala Val Leu Thr Leu Ile
145                 150                 155                 160

Ile Val Glu Asp Cys Ser Leu Leu Ala Cys Leu Pro Gly Gly Ala Phe
                165                 170                 175

Ile Phe Ala Phe Gln Asp Ser Phe Ala Lys Tyr Arg Ile Leu Ser Gln
            180                 185                 190

Val Phe Phe Phe Phe Phe His Leu Lys Tyr Ile Ile Ser Val Pro Ser
        195                 200                 205

Gly Leu
    210

<210>  199
<211>  202
<212>  PRT
<213>  Homo sapiens

<400>  199

Leu Ile Ser Lys Met Arg Met Met Leu Ala Leu Pro Leu Ser Gly Cys
1               5                  10                  15

Tyr Lys Asn Gln Met Arg Ile Val Leu Trp Lys Met Leu Ala Lys Asp
            20                  25                  30

Gln Val Leu His Val Cys Lys Ile Ile Phe Gln Glu Tyr Pro Gln Ser
        35                  40                  45

Phe Trp Ala Gly Ile Ser Tyr Asn Phe Phe Gln Leu Cys Gly Lys Ile
    50                  55                  60

Leu Tyr Lys Cys Ile Asp Ile Asp Arg Tyr Phe His Ile Ile His Ala
65                  70                  75                  80

Val Met Ile Glu Lys Cys Thr Leu Asn Val Leu Ser Phe Asn Ser Thr
```

85 90 95

Gly Asn Leu Asp Met His Glu Ser Phe Lys Thr Met Leu Gln Thr Ser
100 105 110

Val Ser Phe Arg Ile Leu Cys Leu Phe Leu Thr Pro Asn Pro Lys Met
115 120 125

Thr Lys Trp Glu Asn Met Pro Ala Cys Thr Ser Cys Leu Gly Arg Tyr
130 135 140

Ile Lys Gln Trp Val Glu Asp Trp Ile Lys Glu Arg Gln Lys Ala Phe
145 150 155 160

Thr Gln Val Ile Leu Pro Lys Ile Glu Arg Leu Pro Ala Asn Lys Ile
165 170 175

Gly Arg Ser Leu Pro Ser Ala Ile Gln Arg Asp Ile Gly Asn Lys Gln
180 185 190

Leu Tyr Val Cys Val Val Cys Val Cys Val
195 200

<210> 200
<211> 211
<212> PRT
<213> Homo sapiens

<400> 200

Ile Leu Tyr Gly Phe Phe Ala His His Asn Pro Arg Ala Arg His Lys
1 5 10 15

Leu Met Asn Leu Ser Leu Leu Ser Pro Leu Cys Ile Leu Pro Pro Ile
20 25 30

Ile Leu Thr Pro Ser Ser Pro Leu Asp Phe Tyr Cys Ser Val His Ile
35 40 45

Lys Ile Phe Leu Gly Ser Lys Thr Gln Leu His Pro Thr Leu Cys Arg
50 55 60

Tyr Leu Ser Met Phe Phe Ser Leu Phe Pro Thr Ala Asn Phe Ile Leu
65 70 75 80

His Ile Asp Leu Thr Phe Phe Pro His Ser Leu Thr Lys Leu His Asp
85 90 95

Ser Gln Pro Gln Thr Ser Pro Asn Tyr Tyr Ile Arg Pro Pro Ser Leu
100 105 110

Ser Phe Asn Cys Leu Cys Val Ser Leu Pro Thr Arg Ile Ile Pro Ser
115 120 125

Ile Lys Ile Ser Val Asn Cys His Phe Phe Gln Val Thr Phe Leu Phe
130 135 140

Leu Phe Tyr Leu Lys Met Gln Phe Phe His Ser Ala Ser Leu Ala Leu
145 150 155 160

Gln Pro His Leu Phe Tyr Gly Met His Tyr Ile Glu Phe Val Ile Leu
165 170 175

Leu Gln Ile Leu Thr Ser Ala Gln Ile Leu Phe Glu Val Thr Asn Ser
180 185 190

Ala Ser Ile Tyr Leu Cys Val Asn Gly Ile Leu Leu Glu Ser Arg Cys
195 200 205

Arg Leu Gly
210

<210> 201
<211> 132
<212> PRT
<213> Homo sapiens

<400> 201

Thr Ser Pro Ser Pro Asn Gln Leu Arg Ser Cys Ser Leu Pro Gln Gln
1 5 10 15

Ala Gln Arg Gln Val Leu Leu Pro Phe Pro Thr Glu Arg Arg Leu Leu
20 25 30

Phe Cys Thr Ala Pro Arg Ser Leu Asn Ser Leu Pro Gln Pro Val His
35 40 45

Cys Pro Gln Arg Cys Pro Thr Val Ser Val Cys Val Gly Val Pro Gly
50 55 60

Thr Ala Pro Ser Pro Ser Leu Gly Arg Leu Gly Arg Ala Trp Gly Pro
65 70 75 80

Pro Gly Asp Thr Cys Gly Arg Pro Glu Arg Trp Leu Tyr Leu Gly Asp
85 90 95

Gly Leu Val Glu Asp Arg Pro His Gln Pro Ala Arg Arg Gly Ser Gly
100 105 110

Val Leu Phe Trp Gly Gly Lys Ser Arg Leu His Asp Ile Leu Gly Val
115 120 125

Ser Arg Pro Thr
130

<210> 202
<211> 208
<212> PRT
<213> Homo sapiens

<400> 202

Thr Asn Leu Asn Tyr Phe Arg Ala Met Asn Lys Ile Asn Ser Ile Thr
1 5 10 15

Phe Ile Leu Cys Pro Gln Phe Phe Gln Val Asn Tyr Leu Leu Ala Phe
20 25 30

Asp Tyr Tyr Phe Val Ser His Lys Ile Cys Tyr Glu Ser Met Tyr Arg
35 40 45

Ile Leu Ser Asp Trp Leu Cys Tyr Cys Asn Gln Arg Cys Val Asp His
50 55 60

Pro Val Gln Cys Trp Gln Asp Ile Pro Tyr Ile Met Asn Phe His Ser
65 70 75 80

Pro Leu Leu Ala Val Cys Gly Leu Thr Asn Lys Tyr Ser Ile Leu Ile
85 90 95

Leu Gln Ala Ile Arg His Phe Ala Glu Cys His Leu Ser Ile Leu Ser
100 105 110

Lys Ile Leu Phe Phe Leu Glu Ser Asp His Lys Phe Arg Lys Ile Thr
115 120 125

Lys Met Lys Leu Ile Val Phe Val Leu Pro Lys Leu Cys Leu Ser Cys
130 135 140

Leu Leu Lys Gln Ile Thr Glu Lys Asn Glu Ala Tyr Ile Lys Lys Phe
145 150 155 160

Gln Asn Gln Ile Cys Pro Arg Lys Val Thr Leu Phe Leu Ser Ile Ile
165 170 175

Leu Lys Ile Gln Ser Ile Ser Ser Lys Leu Ile Leu Ile Asp Val Phe
180 185 190

Lys Leu Leu Arg Leu Asn Asn Tyr Ile Gln Leu Ser Glu Leu Asp Ser
195 200 205

<210> 203
<211> 94
<212> PRT
<213> Homo sapiens

<400> 203

Glu Pro Gly Val Leu Asp His Leu Cys His His Thr Val His Pro Leu
1 5 10 15

Cys Thr Asn Pro Tyr Tyr Pro Lys Thr Lys Lys His Leu Leu Phe Phe
20 25 30

Ser Ser Cys Asn Leu Phe Ser Asn Lys Leu Ile Leu Gln Ala Gly His
35 40 45

Leu Ser Asp Ile Ser Arg Ile Cys Ile Ile Phe Leu Tyr Leu Tyr Asn
50 55 60

Lys Ile Leu Ala Ser Gly Phe Ser Arg Gln Cys Tyr Leu His Tyr Phe
65 70 75 80

Thr Ile Cys Val Tyr Cys Glu His Tyr Cys Ile Leu Ser Tyr
85 90

<210> 204
<211> 157
<212> PRT
<213> Homo sapiens

<400> 204

Ser Ala Lys Ser Ser Leu Thr Ser Leu Ala Leu Ser Val Leu Gly Lys
1 5 10 15

Leu Ala Asn Ser Asn Arg Trp Gln Leu Arg Leu Val Phe Pro Ala Met
20 25 30

Val Ile Leu Arg Leu Ser Val Ile Leu Leu Thr Ala Cys Leu Ile Lys
35 40 45

Met Pro Glu Ser Tyr Val His Val Ser Arg Val Ser Leu Lys Gly Asn
50 55 60

```
Gly Ser Leu Ser Thr Gly Ala Cys Gln Ser Phe Pro Ser His Ala Met
65                  70                  75                  80

Phe Asp His Val Thr Leu Ser Phe Ile Val Arg Gly Glu Pro Arg Thr
                85                  90                  95

Ser Leu Trp Ser Leu Lys Glu Met Arg Ala Gln Val Ile Leu Lys Arg
            100                 105                 110

Ser Tyr Phe Ser Lys Gly Lys Ser Leu Leu Phe Ala His Ser Ser His
        115                 120                 125

Leu Met Ile Leu Lys Tyr Phe Val Leu Asp Ser Phe Arg Asn Phe Val
    130                 135                 140

Thr Val Gly Glu Ile Ala Thr Tyr Val Ser Ser Val Leu
145                 150                 155
```

<210> 205
<211> 209
<212> PRT
<213> Homo sapiens

<400> 205

```
Pro Leu Leu Ser Trp Val Arg Ile Ala Phe Glu Ile Arg Ile His Leu
1               5                   10                  15

Phe Leu Leu Pro Leu Leu Ile Pro Ser Phe Cys Tyr Ser Val Ile Val
            20                  25                  30

Tyr Phe Leu Ser Lys Thr Leu Gly Arg Ala Leu Gln Leu Leu Leu Asn
        35                  40                  45

His Glu Thr Ser Phe Asn Leu Ser Ser Val Gln Ile Gln Phe Leu Lys
    50                  55                  60

Ile Glu Met Phe Leu Pro Thr Tyr His Phe Tyr Phe Leu Cys Val Val
65                  70                  75                  80

Lys Ile Lys Arg Leu Asp Lys Phe Asp Ile Thr Val Met Ile Thr Gly
                85                  90                  95

Lys His Lys Gly Ile Asn Phe Ala Phe Ser Leu Glu Asn Pro Ser Val
            100                 105                 110

Phe Phe Thr Ile Val Arg Arg Asn Tyr Thr Asp Leu Arg Arg Glu Ala
        115                 120                 125

Asn Glu Asn Phe Leu Ala His Thr Trp Ala Ser Phe Lys Leu Phe Tyr
    130                 135                 140

Phe Leu Ser Tyr Ile Ile Glu Ser Tyr Gln Lys Ile Phe Met His Ile
145                 150                 155                 160

Gln Leu Lys Tyr Lys Tyr Lys Tyr Met Tyr Val Cys Val Ser Thr Thr
                165                 170                 175

Tyr Ile Tyr Ser Asn Asn Lys Arg Lys Phe Val Pro Val Ile Lys Cys
            180                 185                 190

Ser Ser Gln Ile Cys His Thr Val Lys Gly Leu Leu Cys Ser Leu Asn
        195                 200                 205
```

His

<210> 206
<211> 170
<212> PRT
<213> Homo sapiens

<400> 206

Val Leu Asn Leu Phe Tyr Tyr Trp Leu Leu Val Phe Tyr Cys Asp Val
1 5 10 15

Ser Leu His Thr Leu His Phe Phe Cys Asn Thr Phe Gly Leu Phe Leu
20 25 30

Ile Asp Leu Phe Leu Asn Gly Ser Arg Phe Tyr Leu Leu Tyr Ala Leu
35 40 45

Ile Gly Phe Ser His Cys Cys Leu Pro Phe Asn Leu Ile Leu Trp Ile
50 55 60

Phe Leu Ser Ile Arg Lys Pro Phe Ala Val Lys Cys Leu Ile Leu Pro
65 70 75 80

Phe Gly Phe Cys Cys Glu Gln Thr Ser His Leu Lys Val Leu Ser Leu
85 90 95

Ser Val Ile His Ile Cys Leu Tyr Phe Leu Leu Gly Leu Phe Phe His
100 105 110

Phe Lys Thr Leu Phe Asp Leu Gly Leu Leu Phe Val Cys Gly Glu Arg
115 120 125

Gln Asp Pro Asp Leu Ile Leu Phe Gln Gly Val Ser Cys Leu Ser Gln
130 135 140

Asp His Phe Leu Asn Ser Pro Asp Pro Leu Leu Asp Ser His Leu Ala
145 150 155 160

Tyr Leu Ile Cys Thr Leu Pro Ala Asn Ile
165 170

<210> 207
<211> 196
<212> PRT
<213> Homo sapiens

<400> 207

Leu Asn Tyr Asn Arg Gly Leu Thr His Asp Glu Ser Thr His His Lys
1 5 10 15

Ala Phe Ser Gln Ile Ala Cys Phe Leu Val Phe Ile Val Gly Tyr Phe
20 25 30

Val Phe Tyr Tyr Arg Pro Gln Cys Val Leu Lys Cys Pro Phe Val Asp
35 40 45

Ser Thr Lys Arg Gly Phe Pro Thr Cys Cys Val Lys Thr Lys Phe Leu
50 55 60

Cys Glu Ile Asn Pro Cys Ile Thr Lys Cys Phe His Arg Tyr Phe Ser
65 70 75 80

```
Asn Phe Asn Pro Gly Val Phe Ser Phe Ser Leu Ala Thr Met Gly Ser
                85                  90                  95

Glu Thr Ser Phe Cys Arg Phe Tyr Thr Lys Arg Phe Ala Ala Glu Ser
            100                 105                 110

Lys Lys Arg Arg Asn Ile Arg Ile Asp Thr Ser Gln Ser Ile Phe Thr
        115                 120                 125

Glu Ser Leu Phe Leu Val Phe Ile Thr Gly Tyr Val Phe Arg Tyr Arg
    130                 135                 140

Pro Cys Thr Pro Lys Cys Pro Phe Val Asp Ser Thr Lys Arg Val Phe
145                 150                 155                 160

Leu Ala Cys Val Lys Glu Lys Val Val Cys Glu Met Asn Thr Arg Ile
                165                 170                 175

Thr Lys His Phe Tyr Thr Glu Leu Val Pro Ser Phe Tyr Arg Gly Ile
            180                 185                 190

Phe Cys Phe Ser
        195
```

<210> 208
<211> 165
<212> PRT
<213> Homo sapiens

<400> 208

```
Ile Gly Ser Gly Ser Phe Cys Val Asn Ser Val Leu Arg Leu Val Phe
1               5                   10                  15

Phe His Lys Met Cys Thr Ser Ser Asp Leu Gly Ser Ile Leu Ser Cys
            20                  25                  30

Ser Tyr Leu Ala Asp Lys Lys Thr Glu Asp Gln Arg Lys Lys His Arg
        35                  40                  45

Glu Ser Leu Pro Ser Gln Asn Arg Ser Ser Ser Gly Thr Ser Val Ser
    50                  55                  60

Leu Ala Glu Glu Pro Thr Lys Ser Leu Pro Ser Thr Ile Lys Thr Asn
65                  70                  75                  80

Leu Pro Lys Arg Trp Tyr Tyr Gln Pro Ser Met Gly Ser Ala Ser Met
                85                  90                  95

Asp Ser Thr Asn Gln Gly Ser Lys Ile Phe Arg Lys Arg Ser Val Ser
            100                 105                 110

Ile Leu Asn Met Tyr Arg Leu Phe Phe Phe Phe Leu Ile Pro Glu Thr
        115                 120                 125

Ile Gln Tyr Asn Asn Tyr Leu His Asn Ile Tyr Ile Val Leu Gly Val
    130                 135                 140

Val Ser Asn Leu Glu Val Ile Ser Val Gln Met Phe Gly Gly Tyr Ile
145                 150                 155                 160

Gln Ile Leu Cys His
                165
```

<210> 209

<211> 159
<212> PRT
<213> Homo sapiens

<400> 209

Ala Asn Thr Pro Lys Met Ser Pro Pro Ile Ser Phe Pro Asp Val Ser
1 5 10 15

Thr Pro Asn His Cys Ser Ser Leu Tyr Cys Phe Leu Ala Gln His Leu
20 25 30

Thr Leu Phe Val Asp Ile Ile Asn Ile Cys Asn Tyr Phe Pro Tyr Leu
35 40 45

Phe Thr Gly Phe Glu Phe Asp Ser Leu Pro Leu Val Asn Cys Phe Ser
50 55 60

Val Ser Val Leu Phe Ser Ile Ile Ser Pro Ala His Gly Leu Val Ser
65 70 75 80

Ser Thr Tyr Thr Ser Ile Asn Ile Cys Cys Met Asn Ile Cys Asp Gly
85 90 95

Val Glu Thr Lys Ser Leu Phe Ser Phe Met His Leu Ser Val Cys Ile
100 105 110

Met Cys Thr Asp Ser Tyr Ile Glu Ile Met Thr Ala Glu Leu Met Glu
115 120 125

Gly Val Glu Glu Gly Pro Gly Gly Gln Glu Leu Leu Ser Leu His Arg
130 135 140

Cys Glu Ala Asn Pro Ala Pro Thr Cys Lys Asn Leu Val Leu Thr
145 150 155

<210> 210
<211> 152
<212> PRT
<213> Homo sapiens

<400> 210

Gly Ile His Pro Val Val Arg Ala Gly Val Ser Met Glu Glu His His
1 5 10 15

Ser His Lys Glu Arg Gly Asp Pro Thr Pro Arg Ala Arg Ser Arg Ala
20 25 30

Leu Arg Gly His Trp Val His Gln Ala Leu Pro Ala Ser Phe Cys Ser
35 40 45

Pro Asn Ser Gln Gly Pro Pro Val Leu Ser Thr Trp Leu Pro Cys Trp
50 55 60

Ser Glu Lys Ser Ser Ser Gly Ser Ala Leu Pro Pro Val Asn Ile Arg
65 70 75 80

Pro Gly Leu Asn Leu Thr Thr His Ile Gly Val Leu His Pro Val Leu
85 90 95

Asn Phe Pro His Tyr Met Val Thr Ile Pro Arg His Phe Ser Ser His
100 105 110

Leu Cys His Val His Trp Gly Ser Gly Asp Thr Ser Thr Cys Trp Val

115 120 125

Glu Gln Lys Gln Asn Gly Phe Ile Arg Phe Cys His Trp Thr Pro Leu
130 135 140

Ala Glu Ser Val Gly Arg Pro Arg
145 150

<210> 211
<211> 166
<212> PRT
<213> Homo sapiens

<400> 211

Phe Pro Ser Ser Arg Cys Ala Asp Ser Pro Arg Ser Leu Ser Ala Pro
1 5 10 15

Arg Arg Asn Ala Cys Pro Arg Lys Gly Gly Gly Arg Glu Arg Gly Glu
20 25 30

Glu Gly Glu Ser Arg Ser Gly Gly Glu Gly Gly Arg Arg Ala Arg Trp
35 40 45

Ser Ala Glu Lys Ala Glu Lys Arg Asp Glu Gly Glu Arg Ala Glu Gly
50 55 60

Lys Asp Arg Arg Glu Arg Gly Arg Glu Phe Leu Gly Pro Gly Pro Phe
65 70 75 80

Thr Arg Ser Val Trp Gln Val Pro Arg Arg Pro Arg Thr Gly Leu Ala
85 90 95

Lys Pro His Arg Leu Leu Pro Gly Trp Leu Pro Asp Gln Gly His Ala
100 105 110

Glu Val Gly Ala Cys Pro Glu Ala Thr Pro Gly Gln Ala Glu Lys Glu
115 120 125

Gly Thr Arg Asp Phe His Ala Ser Gly Asn Ile Thr Val Gly Trp Ala
130 135 140

Thr Ser Ala Ala Ile Ile Arg Glu Ser Pro Leu Pro Gln Ala Trp Pro
145 150 155 160

Leu Pro Arg Ser Ile Ile
165

<210> 212
<211> 225
<212> PRT
<213> Homo sapiens

<400> 212

Lys Tyr Arg Asp Thr Arg Asn Leu Asn Pro Gly Thr His Cys Gln His
1 5 10 15

Ile Ser Asn Gly Arg Gln Gly Val Ile Glu Thr Lys Gly Trp Lys Ala
20 25 30

Leu Phe Phe Cys Pro Trp Val Phe Thr Asp Trp Phe Cys Pro Glu Gln
35 40 45

Val Leu Ser Thr Lys Ile Phe Val Ala Ile His Gly Lys Ile Gln Gln

50 55 60

Leu Cys Tyr Asp Cys Cys Tyr Leu Leu Tyr Cys Tyr Cys Phe Ile Ser
65 70 75 80

Ser Leu Ile Asp Leu Lys Ile Leu His Leu Met Val Lys Leu Asp Phe
85 90 95

Leu Phe Cys Gln Phe Tyr Leu Asn Asn Leu Leu His Tyr Ile Gln Gly
100 105 110

Lys Ile His Ser Lys Ile Asn Arg Arg Arg Glu Gly Tyr Ala Gln Ser
115 120 125

Ser Ser Val Lys Leu Ser Thr Pro Lys Val Thr Val Gly Ala Ser Gln
130 135 140

Asp Phe Phe Lys Asn Gln Lys His Cys Leu Cys Ser Lys His Leu Thr
145 150 155 160

Ser Ser Glu Leu Ala Tyr Lys Val His His Met Gln Glu Ser Leu Leu
165 170 175

His Ile Lys Phe Ile Ile Met Ile Trp Phe Ile Phe Gly Tyr Ser Asp
180 185 190

Arg Tyr Ser Phe Phe Ile Asn Pro Val Gly Arg Pro Lys Ser Ile Ser
195 200 205

Val Val Leu Gln Cys Leu Tyr Cys Leu Ser Pro Ile Phe Leu Cys Thr
210 215 220

Phe
225

<210> 213
<211> 195
<212> PRT
<213> Homo sapiens

<400> 213

Tyr Pro Ala Leu Ser Val Tyr Asp Ala Ile Ser Val Leu Cys Ser Asp
1 5 10 15

Leu Ser Asp Cys Arg Lys Arg Ile Asn Phe Phe Asn Ala Val Glu Thr
20 25 30

Leu Asn Arg Tyr Arg Gln Ser Ile Phe Thr Phe Ser Tyr Ile Ser Ile
35 40 45

Ile Leu Lys Met Arg Thr Phe Gln Lys Ser Ile Ile Gln Val Tyr Ser
50 55 60

Lys Met Cys Arg Asn Asn Ser Cys Phe Thr Gly Asp Ser Pro Lys Asp
65 70 75 80

Met Cys Leu Glu Val Leu Val Ser Ile Arg Phe Ser Ser Gln Ala Lys
85 90 95

Asp Ser Leu Glu Pro Met His Leu Trp Leu Ile Phe Trp Asp Lys Asn
100 105 110

Lys Ala Arg Asn Gly Glu Ala Tyr Ser Ile Ser Leu Lys Ile Ser Ala
115 120 125

```
Phe Lys Ile Lys Thr Leu Leu Lys Leu His Ile Leu Phe Ser Cys Ile
    130                 135                 140

Cys Phe Tyr Cys Phe Val Asn Tyr Asn Ser Ser Ile Lys Arg Asn Arg
145                 150                 155                 160

Thr Tyr Ala Ile Leu Ser Cys Asp Ser Pro Arg Thr Phe Ser Lys Leu
                165                 170                 175

Phe Tyr Leu Ile Ala Leu Ser Leu Ile Met Gly Ile Ser Ser Leu Asn
            180                 185                 190

Cys Cys Ser
        195
```

<210> 214
<211> 133
<212> PRT
<213> Homo sapiens

<400> 214

```
Arg Thr Gly Lys Arg Asn Ala Met Thr Leu Ile Asn Ile Lys Leu Glu
1               5                   10                  15

Phe Cys Ser Gly Gln Asn Thr Ser Arg Gln Gly Ser Ile Thr His Ser
            20                  25                  30

Val Ser Thr Ser Phe Phe Ile Ser Leu Phe Ile Ser His Met Cys Leu
        35                  40                  45

Ser Gly Ile Pro Ser His Asn Leu Val Thr Tyr Leu Ile Thr Arg Leu
    50                  55                  60

Ser Thr Gln Cys Phe Ala His Arg Lys Cys Ser Val Tyr Ala Ser Ser
65                  70                  75                  80

Pro Gly Cys Leu Cys Arg Val Val Tyr Tyr Gln Asn Ala Leu Tyr Ser
                85                  90                  95

Leu Phe Lys Ala Ser Leu Tyr His Val Gly Met Ile Leu Lys Thr Val
            100                 105                 110

Asn Val Lys Cys Leu Thr Tyr Ser Ser Asp Pro Leu Leu Arg Asn Val
        115                 120                 125

Leu Arg Arg Thr Val
    130
```

<210> 215
<211> 219
<212> PRT
<213> Homo sapiens

<400> 215

```
His Asn Cys Gly Lys Asp Leu Ser Gln Gly Pro Gly Tyr Gln Tyr Ala
1               5                   10                  15

Ser Cys Tyr Leu Gly Met Met Tyr Phe Lys Lys Phe Ile Val Ile Ile
            20                  25                  30

Glu Asn Trp Leu Phe Ile Pro Asn Ile Leu Asn Phe Leu Phe Ile Gly
        35                  40                  45
```

Ser Phe Asn Lys Met Tyr Tyr Ile Leu Ser Leu Asn Leu Val Arg Pro
50 55 60

Lys Ile Val Glu Pro Phe Phe Val Phe Ala Phe Asp Asp Pro Gly Ser
65 70 75 80

Leu Thr Leu Ile Ser Ile Leu Tyr His Asn Lys Asn Ile Gln Asn Tyr
85 90 95

Cys Cys Ile Thr Ile Pro Ser Ser Ser Ala Val Leu Cys Tyr Leu Ser
100 105 110

Phe Thr Ala Val Met Pro Leu Ser Ala Phe Tyr Ser Phe Leu Arg Pro
115 120 125

Pro Asn Phe Pro Leu Pro Val Cys Leu Tyr Leu Gly Asp Gln Ser Ser
130 135 140

Asn Leu Leu Cys Leu Lys Glu Gln Leu Gly Phe Glu Gly Pro Ser Ser
145 150 155 160

Leu Phe Cys Glu Ser Val Gly Thr Leu Val Tyr Gly Leu Gln His Val
165 170 175

Phe Gln Leu Leu Asn Ser Phe Cys Leu Gly Leu Thr Gly Leu Cys Ser
180 185 190

Tyr Leu Met Ser Pro Asp Asn Leu Pro Asp Lys Ser Val Thr Gly Leu
195 200 205

Glu Phe Cys Leu Cys Arg Leu Pro Val His Cys
210 215

<210> 216
<211> 211
<212> PRT
<213> Homo sapiens

<400> 216

Asn Leu Tyr Pro Arg Arg Lys Ala Asp Arg Trp Ile Asp Met Asn Asn
1 5 10 15

Val Ile Ser Leu Phe Ala Ser Glu Lys Leu Glu Thr Gly Glu Lys Met
20 25 30

Gln Ser Val Tyr Pro Thr Pro Gln Arg Gly Arg Val Ile Phe Trp Leu
35 40 45

Leu Lys Tyr Cys Gln Lys Met Tyr Leu Leu Phe Ile Thr Tyr Ser Ser
50 55 60

Ile Ser Phe Val Asn Trp Leu Ile Pro Lys Asn Leu Leu Glu Phe Asn
65 70 75 80

Gly Ser Ser Cys Asp His Thr Gln Gly Ile Thr Ile Ile Tyr Thr Phe
85 90 95

Ile Gly Tyr Cys Ser Ala Asn Ile Asn Asn Ile Val Thr Arg Asp Leu
100 105 110

Gln Gln Glu Lys Arg Lys Arg Phe Phe Lys Cys Ser Lys Gly Lys Lys
115 120 125

```
Arg Glu Lys Ile Leu Met Thr Lys Ser Ile His Pro Arg Glu Lys Thr
    130                 135                 140

Asn Asp Lys Thr Glu Arg Gly Arg Glu Gly Ala Thr Leu Arg Glu Gly
145                 150                 155                 160

Leu Met Gly Asp Glu Arg Tyr Leu Trp Gly Ser Ser Leu Phe Trp Ala
                165                 170                 175

His Tyr Cys Leu Ser Pro Val Ala Pro Gln Arg Leu Pro Pro Gly Leu
            180                 185                 190

Cys Ser Gln Met His Val Tyr Ser Pro Cys Thr Gln Leu Ser Glu Thr
        195                 200                 205

Ser Ser Val
    210
```

<210> 217
<211> 187
<212> PRT
<213> Homo sapiens

<400> 217

```
Ser Ser Phe Val Ser Phe Ser Phe Trp Trp Leu Leu Ala Ile Leu Gly
1               5                   10                  15

Val Pro Trp Leu Val Asp Thr Ser Pro Gln Ser Leu Leu Leu Ser Ser
            20                  25                  30

His Gly His Leu Pro Tyr Val Ser Val Phe Phe Pro Val Ser Tyr Lys
        35                  40                  45

Thr Ser Val Ile Arg Phe Lys Ala His Pro Ile His Asp Asp Leu Ile
    50                  55                  60

Ser Arg Ser Leu Ser Leu Cys Leu Gln Ser Ser Phe Ser Lys Gly His
65                  70                  75                  80

Asn Leu Lys Phe Val Asn Val Ser Leu Gly Ala Arg Arg Met Leu Phe
                85                  90                  95

Asn Leu Leu Lys Thr Thr Tyr Leu Val Phe Arg Ile Leu Lys His Ala
            100                 105                 110

Ser Val Cys Met Tyr Ile Val Arg Trp Ile Tyr Arg Ser Tyr Tyr Leu
        115                 120                 125

Val Leu Thr Lys Leu Ile Phe Thr Lys Tyr Thr Ser Gly Ser Lys Asn
    130                 135                 140

Phe Arg Gln Lys His Pro Thr Tyr Thr Gln Gln Ser His Lys Pro Lys
145                 150                 155                 160

Arg Ile Gly Lys Leu Lys Gly Leu Leu Ser His Pro Leu Tyr Lys Leu
                165                 170                 175

Phe Val Ser His Lys Leu Pro His Asn His Thr
            180                 185
```

<210> 218
<211> 206
<212> PRT
<213> Homo sapiens

<400> 218

Thr Ser Asn His Ser Val Ile Arg Leu Ile Leu Tyr Leu Thr Ser Ser
1 5 10 15

His Gln Asn Tyr Phe Ser Asn Cys Arg Thr Asn His Val Ser Leu Lys
20 25 30

Phe Leu Ile Arg Ala Asp Leu Ser Val Gly Leu Gln Thr Leu Thr Val
35 40 45

Arg Pro Gln His Thr Phe Pro Ala Leu Ser Ser Leu His Thr Val Leu
50 55 60

Trp His Glu Ser Thr Ile Ala His Gly Ser Ile Thr Cys Ser Leu His
65 70 75 80

Thr Met Gln Leu Cys Ser Phe Cys Phe Glu Gly Phe Pro Pro Ala Leu
85 90 95

Leu Asp Arg Ser Glu Pro Thr Leu His Gly Pro Ala His Arg Pro Thr
100 105 110

Pro Leu Asn Leu Phe Phe Leu Leu Pro Ile His Gly Gly Leu Ile Cys
115 120 125

Cys Glu Ser Lys Arg Thr Ser His Cys Cys Cys Asn Pro Tyr Ser Leu
130 135 140

Glu Phe Tyr Glu Asn Tyr Val Asn Ser Glu Leu Leu Lys Val Leu Ala
145 150 155 160

Arg Gly Ser Gly Ser Leu Tyr Phe Cys Ile Leu Ile Ser Pro Ser Pro
165 170 175

His Ser Asp Leu Leu Phe Asn Asp Tyr Pro Ser Met Ser Pro Ser Arg
180 185 190

Asn Ser Ile Arg Ser Phe Pro Lys Tyr Gln Pro Asn Thr Thr
195 200 205

<210> 219
<211> 149
<212> PRT
<213> Homo sapiens

<400> 219

Trp Leu Cys Val Ser Val Gln Lys Arg Leu Arg Gly Arg His Gly Ala
1 5 10 15

Thr Val Gln Glu Ser Leu Gly Leu Leu Thr Ala Thr Ser Gln Pro Leu
20 25 30

Pro Gly Arg Thr Pro Arg Ser Gly Cys Gln Gly Arg Gly Gly Pro Trp
35 40 45

Pro Gly Ser Leu Gly Pro Gly Glu Leu Pro Val Leu Pro Ala Gln Ser
50 55 60

Pro Pro Gly Cys Cys Arg Leu Leu Ala Thr Pro Thr Ser Gln Ala Trp
65 70 75 80

Arg Glu Ala His Ser Cys Cys Cys Thr Thr Leu Val Asn Val Trp Gly

85 90 95

Glu Ala Trp Ala Trp Pro Ala Pro Leu Pro Gly Leu Gln Thr Pro Ala
100 105 110

Gln Pro Gln Tyr Leu Lys Glu Pro Gln Trp Ser Gln Ala Arg Asp Val
115 120 125

Glu Asn Ser Gly Phe Gln Glu Thr Leu Ala Leu Leu Leu Ala Ala Pro
130 135 140

Gly Gly Phe Gln Leu
145

<210> 220
<211> 101
<212> PRT
<213> Homo sapiens

<400> 220

Leu Ala Gly Phe Pro Ser Pro Gly Gly Cys Ser Ala Asp Ser Leu Ser
1 5 10 15

Gly Trp Leu Arg Leu Gln Pro Ala Ala Ile Val Cys Leu Pro Glu Lys
20 25 30

Ser Ile Ala Asp Glu Pro Gly Ala Leu Gly Glu Arg Glu His Thr Glu
35 40 45

Ser Phe Leu Thr Ile Ser Pro Ala Glu Ser Tyr Ile Gly Ala Ala Thr
50 55 60

Pro Tyr Leu Val Leu Ser His Cys Leu Ser Glu Gly Val Leu Gly Leu
65 70 75 80

Pro Gln Ala His Ser Lys Met Ser Pro Val Ala Lys Ala Leu Gly Pro
85 90 95

Asp Ser Arg Pro Phe
100

<210> 221
<211> 215
<212> PRT
<213> Homo sapiens

<400> 221

Thr Trp Thr His Ser Cys Asp Tyr Ile Gln Pro Leu Gly Trp Leu Lys
1 5 10 15

Trp Arg Arg Pro Arg Ile Ala Pro Leu Thr Cys Leu Ala Val Ala Ser
20 25 30

Gly Trp Gly Lys Gly Thr Leu Ile Leu Leu His Arg Val Ser His Pro
35 40 45

Leu Val Glu Thr Ile Phe Leu Ala Trp Leu Ser Gln Gly Ser Ile Pro
50 55 60

Arg Met Trp Lys Gly Asn Leu Gln Ser Leu Leu Gln Pro Ser Leu Glu
65 70 75 80

Ser His Thr Lys Phe Leu Pro Leu His Phe Ile Phe Lys Ala Ser His

85 90 95

Lys Ala Thr Leu Asp Phe Gly Val Gly Lys Thr Ala Ala Leu Asp Glu
100 105 110

Asn Thr Ala Trp Val Phe Phe His Cys Cys Ala Cys Gly Cys Ala Phe
115 120 125

Val Leu Phe Leu Asn Ser Cys Tyr Leu Thr Glu Glu Val Val Ser His
130 135 140

Lys Asn Lys Gln Val Leu Asn Gln Ser Thr Val Gln Ile Pro Ala Pro
145 150 155 160

Pro Ser Ser Thr Thr Thr Tyr Leu Ser Gly Leu Tyr Ile Leu Tyr Leu
165 170 175

Phe Tyr Lys Val Leu Lys Thr Val Pro Gly Ala Ile Lys Lys Asp Thr
180 185 190

Gln His Tyr Leu Ser Phe Ser Ser Ile Leu Met Phe Tyr Phe Ser Thr
195 200 205

Pro Leu Tyr Asn Ile Asn Ile
210 215

<210> 222
<211> 127
<212> PRT
<213> Homo sapiens

<400> 222

Ser Lys Arg Ile Ile Pro Glu Leu Ser Ser Pro Gln Gly Met Tyr Glu
1 5 10 15

Asn Pro Arg Glu Trp Ile Asn His Phe Ala Glu Cys Tyr Ala Thr Phe
20 25 30

Thr Thr Val Ile Ile Pro Gln Cys Lys Lys Asp Leu Leu Lys Met Phe
35 40 45

Leu Pro Asn Lys Leu Val Phe Ile His Leu Phe Ile Pro Phe Ser Ile
50 55 60

Asn Leu Leu Ile Ile Ser Val Cys Gln Ala Gln Phe Leu Asp Cys Leu
65 70 75 80

Phe Thr Asn Lys Leu Asp Ser Lys Val Cys Tyr His Asn Gly Met Leu
85 90 95

Phe Pro Trp Gly Lys Thr Arg Thr Met His Lys Gln Val Tyr Asp Thr
100 105 110

His Ile Ile His Lys Gly Lys Leu Met Asn Trp Met Ser Leu Lys
115 120 125

<210> 223
<211> 167
<212> PRT
<213> Homo sapiens

<400> 223

His Val Ser Ser Ser Leu Glu Lys Thr Phe Ile Asn Gly Pro Val Ser

1 5 10 15

Asp Phe Trp Ser Ser Gln Val Phe Ser Ala Pro Tyr Ser Ile Ser Phe
20 25 30

Lys Arg Asp Ala Ile Leu Ser Lys Ser Ser Asn Ser Leu Pro Phe Ser
35 40 45

Asn Thr Asn Met Lys Phe His Phe Thr Thr Lys Pro Ser Asn Arg Gln
50 55 60

Gln Leu Ser Ile Met Leu Lys Phe Thr Ser Phe Tyr Thr Thr Leu Pro
65 70 75 80

Tyr Phe Phe Phe Ser Gln Lys Ala Ser Pro His Leu Ser Asn Leu Gly
85 90 95

Asn Cys Ser Ile Gly Leu Pro Ser Tyr Phe Ser Tyr Leu Asn Ser Leu
100 105 110

Tyr Cys Thr Ile Phe Leu Leu Ser Leu Leu Lys Met Val His Ile Leu
115 120 125

Tyr Pro Met Gln Lys Phe Ser Leu Ser Ser Thr Thr His Thr Lys Ile
130 135 140

Leu Leu Cys Pro Trp Val Phe Ile Phe Arg Arg Leu Phe Ile Leu His
145 150 155 160

Met Ser Pro Phe Ser Tyr Leu
165

<210> 224
<211> 235
<212> PRT
<213> Homo sapiens

<400> 224

Arg Pro Gly Ala Trp Leu Ala Gly Pro Cys Cys Trp Arg Cys Arg Ala
1 5 10 15

His Pro Phe Val Val Leu Gly Leu Ala Cys Gln Val His Cys Gly Cys
20 25 30

Pro Pro Thr Pro Ser Trp Phe Pro Cys Gly Arg Gly Ala Val Arg Leu
35 40 45

Pro Leu Cys His His His Gln Pro Gly Phe Cys Thr Asp Phe His Ser
50 55 60

His Leu Phe Leu Ala Cys Phe Met Leu Val Leu Thr Gln Ser Ser Ile
65 70 75 80

Phe Ser Leu Leu Ser Met Ala Ile Asn Arg Tyr Leu Ala Ser His Ser
85 90 95

Arg Leu Arg His Lys Ser Leu Val Thr Gly Thr Gln Thr Arg Gly Val
100 105 110

Thr Ala Val Leu Trp Val Leu Ala Phe Gly Thr Gly Leu Thr Pro Phe
115 120 125

Leu Glu Trp Asn Ser Lys Asp Ser Thr Ser Asn Asn Cys Met Glu Pro
130 135 140

Trp Asp Gly Thr Met Asn Glu Ser Cys Cys Leu Val Lys Cys Leu Phe
145 150 155 160

Gln Asn Ala Val Pro Met Ser Tyr Met Val Tyr Phe Ser Phe Gly Gly
165 170 175

Val Leu Pro Pro Leu Leu Val Met Trp Leu Ile Ser Ile Lys Phe Phe
180 185 190

Thr Val Thr Ala Gly Ser Phe Ser Thr Arg Ser Trp Thr Thr Gln Gly
195 200 205

Pro Pro Ser Ser Gly Arg Tyr Thr Gln Pro Ser Arg Trp Leu Trp Trp
210 215 220

Gly Met Phe Ala Leu Cys Ser Leu Pro Val Arg
225 230 235

<210> 225
<211> 209
<212> PRT
<213> Homo sapiens

<400> 225

Gln Glu Thr Gly His Ala Leu Cys Gln Ala Ala Ser Ser Thr His Ala
1 5 10 15

Ala Pro Phe Gln His Leu Cys Ser Ser Ile His Ala Leu Lys Ser Leu
20 25 30

Asn Ser Pro Pro Arg His Gly Leu Pro Ser Arg Ala Gly Met Gly Pro
35 40 45

Phe Leu Val Ser His Ala Arg Ser Pro Pro Glu Ser Cys Met Asn Asn
50 55 60

Arg Leu Asp Pro Cys Phe Gln Ser Glu Asp Thr His Glu Ile Phe Pro
65 70 75 80

Lys Ile Phe Phe Arg Ser Arg His Tyr Cys Glu Tyr His Ile Asn Lys
85 90 95

Leu Ser Leu Phe Gln Phe Leu Phe Lys Trp Arg Ile Ser Ile Ser Gly
100 105 110

Ser Asn Leu Thr Cys Lys Lys Asn Asn Arg Phe Phe Lys Lys Phe Gln
115 120 125

Phe Ile Thr Leu Asn His Ser Tyr Leu Pro Met Leu Gln Cys Thr His
130 135 140

Lys Lys Leu Val Phe Lys Asp Cys His Leu Cys Leu Leu Gly Lys Thr
145 150 155 160

Cys Ile Tyr Pro Ser Phe Leu Lys Asn Ser Ile Met Leu Asn Phe Gln
165 170 175

Ser Asp Ser Val Leu Asp Ser Phe Thr Lys Leu Gln Ser Leu Cys Leu
180 185 190

Gln Ser Tyr Phe Tyr Val Thr Thr Glu Ala Pro Ser Thr Leu Val Ser
195 200 205

Glu

<210> 226
<211> 192
<212> PRT
<213> Homo sapiens

<400> 226

Leu Cys Leu Thr Lys Val Pro Gly Phe Glu Leu Ala Pro Phe Gly Cys
1 5 10 15

Phe Ser Asp Leu Asn Tyr Tyr Thr His Thr His Ile Met Ser Asn Gly
20 25 30

Gln Asn Glu Gly Phe Trp Asp Ser Gly Ile Pro His His Leu Tyr Tyr
35 40 45

Phe Leu Gly Ser Phe Leu Tyr Gln Asn Met Met Cys Leu Ile Trp Ser
50 55 60

Phe Asn Ser Met Ser Asn Tyr Pro Thr Leu Leu Gln Thr Cys Lys Cys
65 70 75 80

Arg Glu Gln Cys Asn Gly Phe Lys Leu Leu Phe Leu His Gly Lys Phe
85 90 95

Cys Leu Gln Lys Gln Met Gln Arg Lys Asp Gly Val Ser Val Ala His
100 105 110

Cys Leu Trp Asn Ile Cys Arg Asp Ser Arg Arg Ala Ile Ile Lys Ile
115 120 125

Ile Gly Thr Glu Ala Leu Val Leu His Ser Thr Ile Leu Tyr Tyr Tyr
130 135 140

Tyr Gly Ile Cys Met His Ser Val Ser Ala Cys Gln Thr Thr Thr Asn
145 150 155 160

Pro Phe Cys Ile Ile Lys Gln Asn Cys Leu Glu Leu Tyr Phe Met Asn
165 170 175

Gln Phe Glu Ser Tyr Ile Ser Leu Phe Arg Leu Ser Gly Leu Leu Gln
180 185 190

<210> 227
<211> 190
<212> PRT
<213> Homo sapiens

<400> 227

Phe Ser Ala Lys Asp Pro Phe Ile Asn Lys Thr Ala Thr Gly Ser Asn
1 5 10 15

Phe Asn Cys Ile Leu Pro Gly Leu Cys Phe Phe Asn Tyr Phe Phe Ala
20 25 30

Val Val Thr Glu Pro Phe His Val Ser Glu Ile His Thr Phe His Ala
35 40 45

Phe Thr Ile Arg Val Trp Pro Val Met Ala Pro Gln Ile Leu Tyr Thr
50 55 60

```
Ile Pro Leu Leu Val His Phe Ile Asn Leu Leu Val Tyr Phe Lys Ser
65                  70                  75                  80

Val Phe Tyr Leu Arg Lys Lys Arg Asn Phe Ser Val Tyr Lys Asp His
                85                  90                  95

Ile Val Leu Pro Tyr Thr Ser Thr Phe Val Tyr Ile Val Tyr Cys Cys
            100                 105                 110

Ile His Thr Ile Val Pro Ser Ser Gln Asp Trp Lys Gln Ser Pro Ala
        115                 120                 125

Thr Pro Thr Val Trp Glu Gly Cys Gln Thr Lys Leu Trp Asp Thr Ser
    130                 135                 140

Pro Gln Asn Ser Gly Leu Lys Leu Val Ser Phe Leu Pro Gln Val Pro
145                 150                 155                 160

Gln Glu Cys Ile Val Thr Val Thr Ala Gly Phe Thr Ser Val Ile Phe
                165                 170                 175

Lys Cys Leu Cys Glu Phe Pro Lys Ser Thr Gln Ser Ser Ser
            180                 185                 190
```

<210> 228
<211> 187
<212> PRT
<213> Homo sapiens

<400> 228

```
Arg Thr Ala Thr Val Gly Ser Val Ser Leu Leu Gln Ser Asp Thr Phe
1               5                   10                  15

Phe Pro Phe Asp Phe Ser Tyr Phe Lys Asn Phe Arg Tyr Cys Ser Tyr
            20                  25                  30

Ala Pro His Val Arg Ile Cys Met Pro Leu Thr Asp Gly Ile Ser Ser
        35                  40                  45

Phe Glu Asp Leu Leu Ala Asn Asn Ile Leu Arg Ile Phe Val Trp Val
    50                  55                  60

Ile Ala Phe Ile Thr Cys Phe Gly Asn Leu Phe Val Ile Gly Met Arg
65                  70                  75                  80

Ser Phe Ile Lys Ala Glu Asn Thr Thr His Ala Met Ser Ile Lys Ile
                85                  90                  95

Leu Cys Cys Lys Tyr Val Ser Ser Ile Ser Arg Leu Arg Ile Ser Ser
            100                 105                 110

Val Ser Cys Ala Leu Asp Ile Tyr Met Tyr Leu Leu Ala Phe Asn Lys
        115                 120                 125

Trp His Leu Met Ile Ile His Pro Gly His Ile Phe Phe Ser Lys Tyr
    130                 135                 140

Lys Ser Ser Gly Ser Leu Trp Leu Cys Phe Arg Leu Tyr Asp Leu Thr
145                 150                 155                 160

Val Ala Cys Ser Gln Glu Tyr Val Leu Gly Met Gly Ala Thr Asn Glu
                165                 170                 175

Ser Ser Asp Arg Leu Ser Phe Val Gly Asp Lys
```

180 185

<210> 229
<211> 210
<212> PRT
<213> Homo sapiens

<400> 229

Glu Leu Lys Gln Lys Thr Ala Pro Cys Leu His Cys Phe Leu Glu Phe
1 5 10 15

His Phe His Glu Thr Tyr Gln Glu Gly Pro Gly Arg Trp Gly Ser Arg
20 25 30

Phe Met Leu Ser Leu Thr Gly Arg Arg Glu Asn Arg Phe Lys Thr His
35 40 45

Arg Asn Gly Glu Ile Ile Ala Arg Glu Cys Trp Arg Thr Thr Gln Gly
50 55 60

Ala Gly Ile Leu Arg Cys Ser Leu Val Leu Cys Glu Ser Arg Ile Ala
65 70 75 80

Gln His Val Gln Met Ser Gly Ala Gly Thr Trp Thr Leu Leu His Val
85 90 95

Pro Val Leu Phe Pro Thr Tyr Pro Glu Cys Gln Pro Ser Pro Gln Ala
100 105 110

Met Ala Val Pro Asn Met Lys Phe Arg Val Arg Val Val Ile Gln Ile
115 120 125

Pro Pro Asn Asn Pro Thr Val Cys Leu Ala Met Ser Ser Phe Leu His
130 135 140

Ser Ser Tyr Leu Asn Ser Trp Ile Val Thr Leu Tyr His Pro Val Ile
145 150 155 160

His Arg Trp Val Ser Thr Glu His Thr Ala Met Arg Ile Pro Gly Trp
165 170 175

His Trp Pro Thr Lys Gln Cys Gln Cys Arg Leu Ala Pro Ala Ser Ser
180 185 190

Lys Gln Thr Ser Pro Val Leu Arg Asp Thr Ser Met Gln Arg Gly Ile
195 200 205

Ser Ala
210

<210> 230
<211> 181
<212> PRT
<213> Homo sapiens

<400> 230

Gly Ser Thr Leu Leu Ala Glu Tyr Thr His His Lys Leu Val Ser Gln
1 5 10 15

Gln Ser Phe Cys Leu Val Phe Met Gly Lys Ile Ile Leu Phe His Arg
20 25 30

Arg His Gln Ser Ala Pro Asn Val His Ile Gln Tyr Thr Thr Glu Arg

35 40 45

Val Phe Gln Thr Cys Ser Met Lys Gly Asn Leu Gln Leu Tyr Glu Leu
50 55 60

Asn Ala Asp Ile Arg Lys Lys Phe Leu Arg Met Leu Leu Ser Thr Phe
65 70 75 80

Tyr Leu Asn Ser Arg Phe Gln Arg Asn Pro Pro Ser Tyr Pro Asn Ile
85 90 95

His Leu Gln Ile Pro Gln Lys Glu Cys Phe Lys Thr Ala Leu Tyr Gln
100 105 110

Trp Gln Ser Ser Thr Leu Leu Val Glu Asp Thr Tyr His Gln Gln Val
115 120 125

Ser Glu Asn Ala Ser Val Tyr Phe Leu Trp Glu Asp Ile Ser Phe Phe
130 135 140

Thr Val Gly Val Lys Ala Ile Glu Met Ser Thr Ser Thr Asn Tyr Lys
145 150 155 160

Lys Ser Val Ser Asn Leu Leu Tyr Glu Arg Pro Cys Ser Ser Leu Val
165 170 175

Glu Trp Lys Tyr Pro
180

<210> 231
<211> 248
<212> PRT
<213> Homo sapiens

<400> 231

Cys His His Thr Gln Thr Ser Gln Ala Phe Leu Thr Leu Val Phe Trp
1 5 10 15

Leu Met Ile Ser Tyr Ala Cys Phe Ile Gly Val Ile Thr Thr Phe Ile
20 25 30

Ser Glu Glu Ser Asn Ile Leu His Leu Ser Ser Val Gln Ala Leu Leu
35 40 45

Tyr Tyr Leu Lys Cys Phe Lys Asn Phe Ser Tyr Leu Phe Ser Leu Leu
50 55 60

Ala Thr Phe His Tyr Ile Cys Leu Leu Cys Phe Arg Ile Leu Ile Tyr
65 70 75 80

Arg Leu Ile Phe Ser Arg Arg Glu Gly Glu Gly Lys Arg Glu Arg Glu
85 90 95

Arg Glu Cys Phe Ser Thr Cys Ser His Val Cys Leu Phe Leu Thr Ala
100 105 110

Phe Thr Gln Ser Ser Arg Leu Ser Gly Ser Lys Gln Gly Leu Tyr Val
115 120 125

Gly Ser Leu Val Phe Gly Ser Ile Ala Asp Pro Val Gln Gly Ala Ala
130 135 140

Ser Ser Ser Leu Tyr Val Val Ser Gly Pro Cys Ala Thr Ser Lys Thr
145 150 155 160

```
Gln Leu Asp Ala Gly Gln Val Thr Pro Glu Thr Ser Gln Leu Pro Val
                165                 170                 175

Ile Arg Ile Glu Leu Gln Ala Thr Ser Ala Lys Gln Ile Gln Ser Leu
            180                 185                 190

Asp Pro Arg Val His Arg Leu Ser Ser Thr Tyr Leu Cys Val Phe Glu
        195                 200                 205

Ile Thr Lys Ala Phe Phe Met Tyr His Ile Trp Val Ile Ile Tyr Ile
    210                 215                 220

Phe Val Ile Leu Leu Leu Trp Phe Gly Tyr Asp Leu Phe Val Pro Thr
225                 230                 235                 240

Lys Thr His Val Glu Ile Arg Ser
                245
```

<210> 232
<211> 163
<212> PRT
<213> Homo sapiens

<400> 232

```
Phe Glu Val Arg Gly Ile Leu Leu Phe Asn Phe Leu Ile Ile Lys Leu
1               5                   10                  15

Phe Leu Arg Thr Ser Leu Lys Val Asn Asp Trp Thr Trp Asp Gln Ala
            20                  25                  30

Pro Lys Lys Ile Asn Pro Val Gln Ile Leu Ser Thr Cys Ser Pro Val
        35                  40                  45

Ala Leu Val Lys Arg Val Gly Ser Leu Met Tyr His Leu Leu Trp Ile
    50                  55                  60

Ser Asn Asn Val Pro Tyr Phe Phe Ile Ile Ala Ser Gly Arg Trp Glu
65                  70                  75                  80

Lys Lys Arg Ser Lys Ser Val Tyr Ser Lys Thr Leu Ser Leu Leu Thr
                85                  90                  95

Phe Gln Lys Asp Phe Met Pro Met Ile Leu Phe Val Phe Leu Val Phe
            100                 105                 110

Thr Ser Thr Asp Phe Ile Met Ser Glu Thr His Leu Asn Leu Ile Leu
        115                 120                 125

Val Pro Gly Ile Phe Pro Leu Met His Gln Thr Ser Gly Ser Ile Leu
    130                 135                 140

Gln Gly Phe Pro Val Ile Cys Gln Thr Thr His Thr Cys Ala Phe Arg
145                 150                 155                 160

Ser Pro Ile
```

<210> 233
<211> 108
<212> PRT
<213> Homo sapiens

<400> 233

```
Lys Ala Phe Leu Lys Ile Leu Leu Ala Gly Thr Cys Tyr Arg Glu Asp
1               5                  10                  15

Ser Ile His Lys Leu Thr Lys Tyr Phe Pro Ser Tyr Ile Phe Ile Phe
            20                  25                  30

Ile Asn Ser Phe Leu Asn Asp Ile Tyr Phe Trp Val Phe Thr His Val
        35                  40                  45

Leu Tyr Met Phe Leu Phe Ser Phe Thr Ile Glu His Thr Leu Tyr Gln
    50                  55                  60

Pro Glu Ala Ser Glu His Leu Met Gly Ala Lys Asn Lys Lys Lys Thr
65                  70                  75                  80

Ser Phe Gly Ile Ala Asn Thr Phe His Leu Cys Leu Ile His Ile Lys
                85                  90                  95

Phe Glu Ser Trp Ala Tyr Tyr Phe Glu His Phe His
            100                 105
```

<210> 234
<211> 145
<212> PRT
<213> Homo sapiens

<400> 234

```
Pro Thr Ser Pro Asn Asn Thr Thr Val Phe Ile Ser Phe Phe Arg Ile
1               5                  10                  15

Val Phe Phe Leu Tyr Ile Leu Glu Leu Cys Val Cys Gly Pro Ile Gln
            20                  25                  30

Asn Ala Leu Leu Tyr Asn Cys Thr Phe Thr Gln Gln Met Phe Leu Ile
        35                  40                  45

Phe Thr His Ala Val Val Cys Ile Arg His Phe Leu Leu Leu Phe Ala
    50                  55                  60

Met Glu Trp Phe Cys Phe Val Phe Val Leu Phe Lys Asn Ala Glu Phe
65                  70                  75                  80

Val Tyr Ser Phe Ser Gly Trp Thr Phe Gly Leu Leu Ser Val Leu Gly
                85                  90                  95

Ser Phe Glu Ser Leu Leu Thr Phe Leu Ser Lys Phe Leu Asn Gly Leu
            100                 105                 110

Pro Leu Leu Leu Thr Leu Arg Ile Pro Met Ser Gly Ile Thr Asp Leu
        115                 120                 125

Val Leu Ser Glu Thr Val Arg Pro Phe Phe Ser Pro Ser Gly Cys Ile
    130                 135                 140

Ile
145
```

<210> 235
<211> 109
<212> PRT
<213> Homo sapiens

<400> 235

```
Trp Thr Ala Trp Asp Pro Ser Ile Phe Gly Val Val Gly Asn Leu Val
1               5                  10                  15

Ala Ile Val Val Leu Cys Lys Ser Arg Lys Glu Gln Lys Glu Thr Thr
            20                  25                  30

Phe Tyr Thr Val Met Arg Leu Ala Ala Thr Asp Leu Leu Phe Thr Leu
        35                  40                  45

Leu Val Ser Gln Val Thr Ile Ala Met Tyr Met Lys Gly Gly Pro Gly
    50                  55                  60

Gly Gln Leu Leu Cys Glu Tyr Ser Ile Phe Ser Leu Phe Phe Phe Ser
65                  70                  75                  80

Gln Ser Gly Leu Ser Ile Val Cys Ala Met Ile Ser Ile Gln Val Ile
                85                  90                  95

Cys Val Arg His Ser Lys Ser Phe Lys Ser Phe Met Phe
            100                 105
```

<210> 236
<211> 181
<212> PRT
<213> Homo sapiens

<400> 236

```
Ser Leu Gly Asp Arg Ala Arg Leu Cys Leu Lys Lys Lys Lys Glu Thr
1               5                  10                  15

Gly Lys Ser Gln Asp Ser Asn His Val Tyr Val Cys Val Cys Thr Ala
            20                  25                  30

Trp Val Leu His Leu Leu Tyr Lys Ile Ile Arg Cys Trp Gln Ile Pro
        35                  40                  45

Arg Pro Val Ala Tyr Val Asn Lys Leu Glu Thr Arg Leu Ser Ala Asn
    50                  55                  60

Leu Val Ala Leu Cys Arg Gly Pro Trp Glu Gly Asn Cys Leu Gln Ile
65                  70                  75                  80

Arg Pro Ser Gly His Gly Ser Gln Ser Leu Gly Trp Thr Pro Lys Thr
                85                  90                  95

His Ser Gly Leu Asn Leu Ala Leu Leu Ser Glu Gln Arg Cys Tyr Lys
            100                 105                 110

Arg Gln Thr His Thr His Arg Ala Ile Arg Ser Ala Leu Val Asn Met
        115                 120                 125

Leu Gly Lys Lys Tyr Asp Thr Leu Ala Tyr Leu Ala Ile Phe Phe Lys
    130                 135                 140

Phe Gln Pro Ser Leu Ile Gly Asp Pro Val Thr His Asp Ser Ser Arg
145                 150                 155                 160

Lys Arg Leu His Phe Leu Phe Ala Asp Lys Glu Ala Glu Leu Glu Phe
                165                 170                 175

Ala Val Gly Arg Asp
            180
```

<210> 237
<211> 208
<212> PRT
<213> Homo sapiens

<400> 237

Ser Thr Arg Thr Thr Pro Leu Glu Arg Glu Ser Ala Phe Thr Asp Ile
1 5 10 15

Asn Leu Ala Pro Gln Lys Phe Leu Val Leu Lys Glu Arg Asp Cys Ile
20 25 30

Trp Thr Leu Ile Pro Lys Glu Lys Glu Pro Glu Thr Asp Asp Ile Lys
35 40 45

Gln Gly Lys Lys Lys Lys Lys Lys Leu Leu Val Ala Gln Lys Gly Val
50 55 60

Asp Gln Ser Leu Asn Tyr Thr Leu Ile Lys Val Asn Tyr Ile Phe Thr
65 70 75 80

Pro Gly Cys Met Trp Trp Ile Leu Ser Ser Phe Leu Leu Val Pro Arg
85 90 95

Cys Ser Leu Ser Gln Trp Lys Leu Leu Gly Glu Lys Gly Gln Glu Val
100 105 110

Leu Ser Phe Leu Ile Trp Pro Leu Ala Pro His Gln His Arg Arg Ala
115 120 125

His His Lys Tyr His Leu Met Ile Phe Phe Pro Arg Ile His Ser Pro
130 135 140

Arg Pro Cys Val Lys Ala Cys Ala Ile Ser Phe Thr Glu Val Leu Leu
145 150 155 160

Ser Leu Gln Val Gly Ser Arg Lys Tyr Gly Ala Arg Lys Thr Leu Lys
165 170 175

Leu Pro Leu Gly Ser Trp Cys Pro Val Met Asp Ala Ile Lys Pro Gln
180 185 190

Thr Gly Trp Cys Ala His Ser His Val Gly Pro Leu Thr Ala Ser Gly
195 200 205

<210> 238
<211> 186
<212> PRT
<213> Homo sapiens

<400> 238

Trp Ala Ser Cys Val Leu Ser Val Cys Met Arg Lys Glu Lys Val Tyr
1 5 10 15

Leu Asn Lys Tyr Tyr Leu Ile Phe Thr Glu Leu Gly Arg Gly Lys Asn
20 25 30

Ala Asn Gln Met Gln Cys Ser Leu Gly Arg Asn Phe Trp Glu Cys Gln
35 40 45

Ser Gly Lys Met Ser Glu Lys Asp Ile Asn Val Pro Leu Lys Lys Ala
50 55 60

Gln Met Glu Leu Thr Phe Gly Thr Ala Ser Lys Gly Gln Thr Phe Pro
65 70 75 80

Gln Tyr Cys Pro Ile Ile Lys Tyr Thr Val Asp Arg Gln Gly Pro Pro
85 90 95

Lys Gln Ser Ile Glu Phe Leu Leu Ile Leu Gly Leu Lys Ile Leu Gly
100 105 110

Lys Val Asn Leu Lys His Ala Glu Ile Trp Cys Glu Ser Gln Lys Arg
115 120 125

Lys Lys Asn Pro Glu Ala Ser Cys Leu Ser His Tyr Leu Pro Pro His
130 135 140

Val Ile Thr Arg Thr Tyr Phe Phe Ser Phe Phe Arg Ser Asn Ala Phe
145 150 155 160

Asp Ser Ser Leu Phe Ala Phe Ile Leu Val His Phe Ile Cys Leu Arg
165 170 175

Val Lys Val Phe Thr Ser Leu Arg Thr Ile
180 185

<210> 239
<211> 213
<212> PRT
<213> Homo sapiens

<400> 239

Trp Ile Phe Ser Lys Val Val Cys Thr Glu Arg Val Glu Gln Lys Ser
1 5 10 15

Lys Thr Cys Asn Asn Ser Glu Ile Phe Gly Phe Val Thr Thr Glu Lys
20 25 30

His Cys Trp Arg Cys Met Val Cys Lys Cys Glu Asn Val Pro Leu Ile
35 40 45

Ala Cys Ile Gln His Glu Gly Leu Leu Phe Val Phe Tyr Phe Ser Asn
50 55 60

Leu Leu Ser Phe Ser Arg Cys Pro Ser His Thr Glu Pro Arg Ser Leu
65 70 75 80

Thr Gly Val Glu Phe Leu Leu Leu Gly Leu Ser Gly Asp Pro Glu Leu
85 90 95

Gln Pro Val Leu Ala Leu Leu Ser Leu Ser Leu Ser Met Tyr Leu Val
100 105 110

Thr Val Leu Arg Asn Leu Leu Ile Ile Leu Ala Val Asn Pro Asp Ser
115 120 125

His Leu His Thr Pro Met Tyr Phe Phe Leu Ser Asn Leu Cys Trp Ala
130 135 140

Asn Leu Ser Phe Thr Ser Ala Thr Val Pro Lys Met Thr Val Asp Met
145 150 155 160

Gln Leu His Ser Arg Val Ile Ser His Ala Gly Cys Leu Thr Gln Met
165 170 175

Ser Phe Leu Val Leu Phe Ala Cys Ile Glu Asp Met Leu Leu Thr Met

180 185 190

Met Ala Tyr Asp Cys Phe Val Ala Ile Leu Ser Pro Ser Ala Leu Pro
195 200 205

Ser His Cys Glu Ser
210

<210> 240
<211> 200
<212> PRT
<213> Homo sapiens

<400> 240

Met Cys Asn Tyr Ser Thr His Gln Leu Tyr His Phe Asn Ser Leu Tyr
1 5 10 15

Ile Val Pro Gln Val Ser Phe Ser Asn Gly His Tyr Gly Leu Ser Thr
20 25 30

Lys Tyr Pro Phe Ser Pro Phe Pro Leu Ile Leu Glu Thr Asp Leu Phe
35 40 45

Ser Tyr Leu Thr Phe Pro Ser Leu Ser Leu Cys Leu Gly Gly Ser Ser
50 55 60

Asn Pro Val Ser Ala Met Cys Phe Ile Val Gln Gly Tyr Phe Ile Cys
65 70 75 80

His Asp Asn Asn Trp Phe Arg Asp Gly Gln Ile Ile Lys Phe Trp Pro
85 90 95

Ile Arg Cys Lys Arg Asp Ser Lys Lys Glu Thr Phe Ser Ile Leu Pro
100 105 110

Leu Val Ser Ser Met Val Leu Leu Lys Val Leu Pro Ser Tyr Glu Ser
115 120 125

Arg Thr Lys Asp Ser Glu Met Ala Arg Lys His Glu Pro Arg Ser Trp
130 135 140

Ile Thr Leu Leu Ile Tyr Tyr Ile Lys Gln Ser Trp Arg Pro His Tyr
145 150 155 160

His Tyr Asn Cys Arg Tyr Val Ile Thr Lys Val Leu Phe Gly Trp Ile
165 170 175

Leu Phe Tyr Phe Leu Gln Val Ser Lys Tyr Leu Thr Ile Cys His Pro
180 185 190

Ile Ala His Leu His Gln Gly Asn
195 200

<210> 241
<211> 195
<212> PRT
<213> Homo sapiens

<400> 241

Leu Ala Asn Thr Asn Gln Asn Val Ser Asn Tyr Pro Ser Phe Leu His
1 5 10 15

Phe Lys Ile Pro Pro Phe Ile Thr His Gln Ile Leu Thr Ser Thr Glu

20 25 30

Ser Leu Ser Gln Phe Ser Ile Leu Phe Tyr Arg Ser Val Gly Leu Phe
35 40 45

Leu Gly Arg Tyr Tyr Lys Met Thr Leu Phe Leu Ile Arg Lys Ala Ile
50 55 60

Lys Ala Tyr Tyr Arg Lys Ile Arg Asn Ile Thr Leu Lys Asn Lys Gln
65 70 75 80

Thr Lys Thr Leu Val Leu Ala Pro Arg Asp Tyr Tyr His Phe Thr Trp
85 90 95

Met Phe Ile Thr Pro Asp His Leu Ile Tyr Ile Asn Val Tyr Lys Tyr
100 105 110

Val His Ser Ser Lys Ile Glu Ile Thr Pro Tyr Lys Trp Phe Cys Lys
115 120 125

Leu Phe Ser Phe His Asn Thr Ser Gly Ile Cys Phe Pro Cys Gln Ile
130 135 140

Val Phe Phe Leu Lys Leu Leu Asn Cys Lys Ile His Ala Tyr Arg Lys
145 150 155 160

Val His Glu Ile Asn Thr Phe Ser Ser Met Ile Tyr His Lys Ala Asn
165 170 175

Thr His Val Thr Thr Thr Gln Val Glu Lys Tyr Asn Ile Val Ser Ile
180 185 190

Pro Gly Ser
195

<210> 242
<211> 225
<212> PRT
<213> Homo sapiens

<400> 242

Tyr Pro Ile Leu Trp His Leu Gly Arg Leu Asn Thr Leu Asp Arg Lys
1 5 10 15

Leu Glu Arg Pro Gln Lys Gln Ala Leu Ser Asp Leu Leu Pro Ser Ser
20 25 30

Cys Ser Ser Val Ser Pro Lys Ser Lys Val Leu Lys Thr Arg Ile Pro
35 40 45

Leu Pro Gln Gly Arg Ser Lys Leu Glu Pro Leu Tyr Pro Lys Ser Asn
50 55 60

His Lys Thr Tyr Lys Cys His Thr Leu Pro Ser Pro Leu Arg Pro Leu
65 70 75 80

Leu Asp Ala Gly Pro Pro Leu Tyr Leu Gly Lys Arg His Pro Ser Gln
85 90 95

Arg Asn Gln Glu Val Ser Glu Gln Arg Gly Leu Leu Val Ser Pro Leu
100 105 110

Leu Trp Phe Gly Tyr Gly Leu Phe Gly Pro Thr Glu Ser Tyr Val Glu
115 120 125

```
Ile Phe Gln Cys Cys Lys Trp Gly Val Val Arg Asp Val Trp Ala Met
    130                 135                 140

Arg Val Asp Pro Ser Val Thr Trp Phe His Ser His Arg Ser Glu Phe
145                 150                 155                 160

Ser Leu Leu Ala Pro Lys Thr Thr Val Cys Lys Glu Pro Asp Thr Ala
                165                 170                 175

Ser Ser Leu Pro Leu Ala Ser Cys Pro Gly Val Pro Leu Tyr Thr Ser
            180                 185                 190

Gly Ser Leu Cys Leu Leu Pro Val Glu Ala Ala Arg Ser Cys Gln Ser
        195                 200                 205

Arg Cys Cys Tyr Ala Ser Gly Met Ala Ser Arg Thr Val Ser His Ile
    210                 215                 220

Phe
225
```

<210> 243
<211> 219
<212> PRT
<213> Homo sapiens

<400> 243

```
Cys Arg Arg Thr Tyr Gly Glu Asn Ser Cys Ile Ala Lys His Glu Ala
1               5                   10                  15

His Val Pro Ser Ser Ser Pro Glu Val Cys Leu Phe Met Leu Pro Gly
            20                  25                  30

Ile Pro Phe Arg Lys Gln Val Asn Gly Ala Phe Cys Thr Phe Met Leu
        35                  40                  45

Asn Gly Glu Pro Lys Arg Val Thr Thr Pro Leu Gln Cys Leu Leu Gly
    50                  55                  60

Leu Gly Glu Gln Arg Ser Cys Lys Tyr Glu Val Leu Lys Asp Ser Val
65                  70                  75                  80

Thr Arg Val Met Ile Phe Gln Tyr Gly Gln Lys Thr Ser Ser Met Gln
                85                  90                  95

Pro Ser Leu Thr Trp Pro Tyr Lys Thr Lys Val Val Trp Pro Glu Leu
            100                 105                 110

Glu Gln Leu Gly Trp Met Ala Gln Cys Lys Gly Ala Gly Gly Arg Pro
        115                 120                 125

Val Asp Pro Thr Leu Gly Trp Pro His Gly Gly Gln Ser Pro Cys Ser
    130                 135                 140

Leu Lys Trp Pro Thr Pro Val Pro Arg Lys Ala Thr Pro Glu Val Pro
145                 150                 155                 160

Thr Ile Cys Cys Asn Gln Ile Cys Asn His Arg Leu Phe Leu Ser Arg
                165                 170                 175

Val Gln Leu Ala Ile Ile Asn Gly Met Asn Gly Ala Pro Gln Met Ser
            180                 185                 190
```

Thr Ala Ser Ser Met Tyr Gly Glu Gln Thr Leu Leu Ser Cys Cys His
195 200 205

Val Gly Ile Ser Val Gln Leu Cys Gln Val Phe
210 215

<210> 244
<211> 213
<212> PRT
<213> Homo sapiens

<400> 244

Ile Phe Tyr Leu Arg Asn Phe Phe Gln Leu His Asn Leu Leu Leu Glu
1 5 10 15

Met Ser Ser Glu Phe Leu Asp Cys Cys Leu Asn Ser Phe Val Arg Ala
20 25 30

Pro Ile Thr Lys Tyr His Arg Leu Gly Asp Leu Tyr Asn Met Asn Leu
35 40 45

Phe Ser Gln Ile Leu Glu Ser Gly Cys Ser Ser Arg Cys Arg Gln Val
50 55 60

Trp Phe Leu Leu Arg Pro Leu Ser Leu Ala His Arg Arg Thr Ser Ser
65 70 75 80

Cys Cys Val Phe Thr Trp Leu Ser Leu Cys Val Cys Leu Cys Pro Asn
85 90 95

Leu Leu Phe Leu Gly His Leu Leu Cys Ser Ile Arg Ala His Leu Asn
100 105 110

Asp Ser Ile Leu Thr Leu Ala Leu Arg Tyr Phe Leu Gln Ile Gln Thr
115 120 125

His Phe Lys Val Leu Arg Arg Arg Phe Asn Phe Met Asn Phe Arg Gly
130 135 140

Asp Thr Asn Gln Leu Ile Thr Gln Cys Tyr Val His Asn Lys Phe Asn
145 150 155 160

Lys Thr Cys Lys Asn Ile Phe Gln Ile Leu Ser Tyr Asn Phe Pro Cys
165 170 175

Ala Val Ile Asp Pro Lys Tyr Ser Glu Leu Leu Thr Phe Leu Ile Trp
180 185 190

Leu Gly Pro His Tyr Ile Ser Leu Leu Pro Ser Leu Cys Arg His Gln
195 200 205

Ser Ser Lys Lys Gly
210

<210> 245
<211> 227
<212> PRT
<213> Homo sapiens

<400> 245

Pro Ser Pro Gln Ser Leu Ser Gln Trp Met Val Leu Lys Asn Thr Cys
1 5 10 15

Ile Glu Cys Ile Leu Val Ser Gly Met Pro Leu Thr Pro Glu Gly Glu
20 25 30

Val Leu Glu Gly Arg Asn Cys Ser Trp Ala Leu Gly Gln Gly Asp Leu
35 40 45

Asp Ser Ser Pro Ala Ser Leu Thr Tyr Trp Leu Trp Ala Asn Tyr Leu
50 55 60

Thr Trp Leu Ser Leu Gly Phe Leu Ile Cys Glu Met Gln Leu Leu Gly
65 70 75 80

Phe Asp Glu Pro Met His Met Arg Leu Glu Glu Tyr Trp Leu Met Gln
85 90 95

Gly Leu Pro Leu Val Leu Ser Leu His Pro Trp Ser Leu Ala Leu Cys
100 105 110

Arg Ala Gly Arg Met Gln Val Leu Gly Arg Trp Ala Trp Leu Met Gly
115 120 125

Val Ala Val Ala Phe Ala Asp Glu Tyr Glu Cys Gln Ala Cys Pro Asn
130 135 140

Asn Glu Trp Ser Tyr Gln Ser Glu Thr Ser Cys Phe Lys Arg Gln Leu
145 150 155 160

Val Phe Leu Glu Trp His Glu Ala Pro Thr Ile Ala Val Ala Leu Leu
165 170 175

Ala Ala Leu Gly Phe Leu Ser Thr Leu Ala Ile Leu Val Ile Phe Trp
180 185 190

Arg His Phe Gln Thr Pro Ile Val Arg Ser Ala Gly Gly Pro Met Cys
195 200 205

Phe Leu Met Leu Thr Leu Leu Leu Val Ala Tyr Met Val Val Pro Val
210 215 220

Tyr Val Gly
225

<210> 246
<211> 221
<212> PRT
<213> Homo sapiens

<400> 246

Val Glu Ser Asn Asp Val Leu Leu Ser His Arg Val Lys Lys Leu Asp
1 5 10 15

Ile Gly Ser Asn Gln Asn Pro His Cys Ile Pro Ser Pro Lys Val Thr
20 25 30

Thr Phe Leu Thr Ser Ile Asp Leu Phe Ile Asn Ser Phe Thr Asp Thr
35 40 45

Ile Ile Ser Tyr Lys Tyr Gln Asn Leu Asp Thr Pro Phe Arg Asn Asn
50 55 60

Phe Asn Gln Val Phe Ser Phe Arg Met Phe Asn Tyr Thr Leu Arg Tyr
65 70 75 80

Ile Tyr Leu Asn Val Cys Leu Phe Lys Tyr Val Asp Tyr Val Leu Leu

85 90 95

Pro Lys Lys Val Leu Lys Leu Leu Pro Ser Leu Ala Ala His Lys Ile
100 105 110

Lys Lys Ser Arg Gln Met Tyr Pro Trp Leu Ala Phe Ser Tyr Gln Gln
115 120 125

Lys Asp Trp Phe Tyr Ser Asn Asn Ile Lys Asn Ala Gly Phe Asn His
130 135 140

Ile Cys Ile Tyr Thr His Thr His Ile Tyr Asp Phe Thr Tyr Ile Ser
145 150 155 160

Tyr Lys Tyr Asp Phe Lys Pro Leu His Leu Tyr Ile Phe Leu Tyr Lys
165 170 175

Tyr Tyr Ile Tyr Phe Ile Phe Tyr Ile Tyr Phe Ile Tyr Phe Tyr Ile
180 185 190

Leu His Thr Phe Tyr Val Tyr Leu Ile Phe Tyr Ile Tyr Leu Tyr Tyr
195 200 205

Ile Tyr Phe Ile Leu Pro Phe Leu Tyr Ile Tyr Thr His
210 215 220

<210> 247
<211> 157
<212> PRT
<213> Homo sapiens

<400> 247

Val Gln Arg Arg Asp Ile Phe Thr His Ile Asn Thr Ile Phe Arg Phe
1 5 10 15

Tyr Leu Ser Tyr Asn Ser Asn Pro Cys His Ser Asp Ser Asn Ile Leu
20 25 30

Ala Phe Glu Ser Ser Ile Met Leu Ala Phe Leu Leu Lys Thr Cys Ser
35 40 45

Ala Phe Lys Thr Gln Ile Ser Tyr Tyr Leu Val Leu Lys His Phe Pro
50 55 60

Thr Leu Leu Val Met Thr Thr Tyr Phe Cys Val Lys Leu Cys Met Tyr
65 70 75 80

Cys Phe Thr Phe Asp Ile Leu Leu Ser Leu Phe Val Cys Met Thr Ala
85 90 95

Phe Phe Phe Leu Leu Asp His Lys Leu Leu Glu Tyr Lys Asn Leu Leu
100 105 110

Ile Phe Ile Ser Ser Val Phe Thr Thr Val Phe Gly Lys Tyr Ser Val
115 120 125

Asn Met Asn Ile Lys Glu Thr Tyr Leu Lys Tyr Val Ile Ile Phe Tyr
130 135 140

Glu Cys Phe Leu Gln Gly Ser Asp Asn Glu Glu Gly Val
145 150 155

<210> 248
<211> 220

<212> PRT
<213> Homo sapiens

<400> 248

Gly His Ile His His Leu Arg Cys Val Val Lys Pro Glu Thr Pro His
1 5 10 15

Thr Tyr Val His Pro Leu Gly Phe Leu Phe Pro Gly Asp Leu Leu His
20 25 30

Phe Cys Pro Lys Met Leu Ala Asn Leu Ile Ser His Ile Lys Ser Ile
35 40 45

Ser Tyr Ala Gly Cys Leu Leu Gln Phe Phe Tyr Phe Ser Met Cys Ala
50 55 60

Ala Glu Gly Tyr Phe Leu Ser Val Met Ser Phe Asp Arg Phe Leu Thr
65 70 75 80

Ile Cys Arg Pro Leu His Tyr Pro Thr Val Met Thr His His Leu Cys
85 90 95

Val Arg Leu Val Ala Phe Cys Arg Ala Gly Gly Phe Leu Ser Ile Leu
100 105 110

Met Pro Ala Val Leu Met Ser Arg Val Pro Phe Cys Gly Pro Asn Ile
115 120 125

Thr Asp His Phe Phe Cys Asn Leu Gly Pro Leu Leu Ala Leu Ser Cys
130 135 140

Ala Pro Val Pro Lys Thr Thr Leu Thr Cys Ala Thr Val Ser Ser Leu
145 150 155 160

Ile Ile Phe Ile Thr Phe Leu Tyr Ile Leu Gly Ser His Ile Leu Val
165 170 175

Leu Arg Ala Val Leu Trp Val Pro Ala Gly Ser Gly Arg Asn Lys Ala
180 185 190

Phe Ser Thr Cys Ala Ser His Phe Leu Val Val Ser Phe Phe Tyr Gly
195 200 205

Ser Val Met Val Met Tyr Val Ser Pro Gly Ser Arg
210 215 220

<210> 249
<211> 180
<212> PRT
<213> Homo sapiens

<400> 249

Ala Ala Ser Cys Thr Ser His Pro Ala Phe Pro Phe Arg Pro Pro Asn
1 5 10 15

Asn Ala Ala Lys Gly Asn Trp Asn Pro Gln Pro Glu Leu Pro Ser Leu
20 25 30

Lys Pro Thr Val Pro His Val Ala His His Thr Ala His Gln Arg Ser
35 40 45

Thr Asn Leu Val Ser Asp Val Val Pro Glu Ile Ile Arg Tyr Ser Gln
50 55 60

```
Pro Glu Pro Val Ser Leu Ala Ser Pro Leu Ile Leu Asn Arg Ile Arg
65                  70                  75                  80

Ser Ser Ala Ala Phe Leu Lys Ala Ala Gly Arg Gln Ser Ser Cys Leu
                85                  90                  95

Thr Leu Phe Ala Trp Trp His Gln Pro Ser Ile Thr Asn Thr Phe Leu
            100                 105                 110

Ser Ser Arg Trp Pro Asp Ser Ile Pro Trp His Ser Pro Gln Gln Ser
        115                 120                 125

Leu Lys Ser Gly Asn Trp Asp His Arg Glu Phe Gln Lys Glu Ile Leu
    130                 135                 140

Ala Asp Ser Lys Thr Arg Asp Arg Pro Ala Ile Leu Glu Arg Ile Pro
145                 150                 155                 160

Val Pro Pro Pro Phe Thr Asp Asn Ser Thr Val Gln Glu Val Met His
                165                 170                 175

Ala Gln Gly His
            180
```

<210> 250
<211> 93
<212> PRT
<213> Homo sapiens

<400> 250

```
Leu Lys Tyr Ser Asn His Asp Ile Cys Glu Phe Ser Met Lys Lys Arg
1               5                   10                  15

Gly Lys Leu Ala Arg Tyr Ser Asp Asp Lys Ser Leu Phe Leu Leu Tyr
            20                  25                  30

Phe Ser Ile Cys Thr Ile Thr Pro Gly Glu Ile Met Glu Met Arg Asn
        35                  40                  45

Thr Thr Pro Asp Phe Ile Leu Leu Gly Leu Phe Asn His Thr Arg Ala
    50                  55                  60

His Gln Val Leu Phe Met Met Val Leu Ser Ile Val Leu Thr Ser Leu
65                  70                  75                  80

Phe Gly Asn Ser Leu Met Ile Leu Leu Ile His Arg Asp
                85                  90
```

<210> 251
<211> 105
<212> PRT
<213> Homo sapiens

<400> 251

```
Arg Leu His Thr Pro Met Tyr Phe Leu Leu Ser Gln Leu Ser Leu Met
1               5                   10                  15

Asp Val Met Leu Val Ser Thr Thr Val Pro Lys Met Ala Ala Asp Tyr
            20                  25                  30

Leu Thr Gly Asn Lys Ala Ile Ser Arg Ala Gly Cys Gly Val Gln Ile
        35                  40                  45
```

```
Phe Phe Leu Leu Thr Leu Gly Gly Gly Glu Cys Phe Leu Leu Ala Ala
    50                  55                  60

Met Ala Tyr Asp Arg Tyr Ala Ala Val Cys His Pro Leu Arg Tyr Pro
65                  70                  75                  80

Thr Leu Met Ser Trp Gln Leu Cys Leu Arg Met Thr Met Ser Ser Trp
                85                  90                  95

Leu Leu Gly Ala Ala Asp Gly Leu Leu
            100                 105
```

<210> 252
<211> 213
<212> PRT
<213> Homo sapiens

<400> 252

```
Met Ser Leu Gly Phe Ser Glu Ile Glu His Phe Gly Gln Ala Val Gly
1               5                   10                  15

Ser Leu Tyr Asp Cys Leu Asp Thr Ala Lys Gly Thr Phe Phe Leu Ser
            20                  25                  30

Pro Asp Ser Glu Val Leu Glu Thr Ala Val Ala Leu Ala Thr Gly Cys
        35                  40                  45

Val Asp His Leu Arg Met Thr Trp Gly Ser Val Leu Cys Thr Leu Glu
    50                  55                  60

Pro Ile Gly Ser Leu Gln Trp Val Pro Trp Cys Thr Gln His Gln Ala
65                  70                  75                  80

Val Arg Thr Thr Pro Asn Gly Leu Gly Gly Arg Ser Lys Thr Thr Gly
                85                  90                  95

Ser Val Pro Val Leu Thr Pro Leu Cys Pro His Arg Pro Gly Leu Gln
            100                 105                 110

Gly Pro Cys Pro Ser Arg Ala Glu Asn Val Val Leu Trp Glu Pro Ser
        115                 120                 125

Gly Pro Leu Gly Pro Gln His Trp Ala Met Gly Ser Ser Leu Pro Glu
    130                 135                 140

Thr Gly Ala Trp Gly Cys Ser Ile Gln Leu Pro Lys Pro Lys Arg His
145                 150                 155                 160

Trp Asp Arg Trp Pro Ser Arg Leu Arg Asp Ala Gln Val Pro Glu Val
                165                 170                 175

Gly Arg Ala Leu Gly Gly Val Pro Thr Ala Ile Leu Gln Ile Gln Lys
            180                 185                 190

Leu Arg Pro Arg Glu Gly Glu Arg Phe Ala Glu His Ala Gln Gln Ala
        195                 200                 205

Ser Gly Arg Ala Gly
    210
```

<210> 253
<211> 206
<212> PRT

<213> Homo sapiens

<400> 253

```
Arg Trp Ala Glu Ser Ile Phe Ile Thr Lys Val Ser Gly Ala Gln Ala
1               5                  10                  15

Lys Pro Ala Ala Phe Gln Gly Lys His Ser Val Leu Val Leu Leu Leu
            20                  25                  30

Asp Cys Leu Ser Glu Val Thr Asp Trp Ile Lys Gln Asn Thr Pro Glu
        35                  40                  45

Ile Phe Thr Lys Lys Val Arg Ser Lys Arg Lys Val Val Lys Gly Asn
    50                  55                  60

Val Leu Ser Asn Gly Trp Leu Met Ser Lys Ser Ser Leu Lys Ile Tyr
65                  70                  75                  80

Leu Phe Ser Ser Phe Arg Lys Ala Thr Glu Met Gln Thr Gly Ala Ile
                85                  90                  95

Asn Asn Ile Val Leu Glu Asp Asn Leu Lys Ile Val Pro Lys Met Pro
            100                 105                 110

Phe Val Thr Val Ile Leu His Leu Asn His Trp Gln Phe Gly Met Thr
        115                 120                 125

Val Phe Cys Thr Ala Arg Cys Thr Leu Tyr Tyr Ile Arg Glu Arg His
    130                 135                 140

Ala Cys Ala Pro Pro Ser Ser Pro His Lys Ser Pro Gly Gly His Lys
145                 150                 155                 160

Asn Val Val Pro Pro Gly Val Ser Lys Asn Leu Thr Arg Lys Tyr Ile
                165                 170                 175

Leu Ile Leu His Leu Gly Asn Val Val Ile Ser Leu Met Leu Ile Phe
            180                 185                 190

Ile Ser Pro Ser Ser Ser Cys Leu Tyr Glu Leu Leu Leu Ser
        195                 200                 205
```

<210> 254
<211> 214
<212> PRT
<213> Homo sapiens

<400> 254

```
Tyr Ala Met Leu His Thr His Cys Trp Trp Leu Pro Ser Ile Ser Tyr
1               5                  10                  15

Ser Val Thr Ile Asn Ser His Phe Ser Leu Ser Pro Tyr Thr Phe Pro
            20                  25                  30

Ser Leu Ser Asp Ala Thr Val Pro Ser Phe Arg Thr Leu Leu Thr Phe
        35                  40                  45

Phe Ser Ala Phe Leu Leu Lys Ile Asn Phe Tyr Leu Leu Thr Leu Tyr
    50                  55                  60

Thr Phe Met Gly Tyr Ser Val Met Phe Gln Val Tyr Thr Leu His Asp
65                  70                  75                  80
```

```
Asp Gln Ile Met Val Ile Thr Val Phe Thr Thr Leu Asn Ile Asp His
                85                  90                  95

Phe Leu Val Val Ile Thr Phe Lys Ile Phe Ser Ser Ser Tyr Leu Lys
            100                 105                 110

Ser Ile His Tyr Ile Val Val Cys Gln Arg His Pro Thr Val Gln Gln
        115                 120                 125

Asn Thr Arg Thr Tyr Ser Ser Leu Leu Cys Thr His Trp Pro Thr Ser
    130                 135                 140

Pro Asp Pro Ser Ser Pro Leu Pro Ser Pro Thr Val His Phe Leu Asn
145                 150                 155                 160

Glu Thr Cys Ile Ser Leu Thr Tyr Leu Ile Tyr Asn Tyr Val Cys Asn
                165                 170                 175

Ser Ile Lys His Ile Ser Asn Trp Pro Asp Thr Cys Leu Leu Ile Ser
            180                 185                 190

Ser Tyr Leu Leu His Tyr Thr Gly Asn Ser Lys Gln Lys Asn Asn Arg
        195                 200                 205

Leu Asn Phe Tyr Leu Val
    210
```

<210> 255
<211> 208
<212> PRT
<213> Homo sapiens

<400> 255

```
Ala Ala Cys Ile Ile Ser Leu Val Thr Leu Asp Arg Glu Thr Arg Leu
1               5                   10                  15

Cys Ser Gly Ser Trp Ala Ser Ala Cys Ala Gly Asn Ala Val Ser Ile
            20                  25                  30

Tyr Ile Leu Asn Leu Ala Ala Ala Asp Phe Leu Phe Leu Ser Gly His
        35                  40                  45

Val Ile Arg Ser Ala Ser Leu Leu Ile Asn Ile Cys His Pro Ile Ser
    50                  55                  60

Lys Ile Leu Ile Pro Val Met Thr Phe Leu Tyr Phe Thr Gly Leu Ser
65                  70                  75                  80

Phe Leu Ser Ala Met Ser Thr Glu Arg Cys Leu Cys Val Leu Trp Pro
                85                  90                  95

Ile Trp Tyr Arg Cys Leu Leu Pro Pro His Thr Cys Gln Arg Ser Cys
            100                 105                 110

Val Ser Cys Phe Gly Pro Cys Pro Tyr Cys Gly Ala Ser Trp Ser Glu
        115                 120                 125

Cys Ser Val Thr Ser Cys Leu Val Met Leu Ile Leu Phe Gly Val Asn
    130                 135                 140

His Gln Ile Ser Ser Gln Ser Cys Gly Phe Phe Tyr Val Trp Phe Ser
145                 150                 155                 160

Val Gly Pro Ala Trp Ser Cys Leu Gly Phe Ser Val Asp Pro Gly Arg
```

```
                165                 170                 175

Cys Leu Pro Gly Cys Thr Arg Ser Cys Ser Gln Cys Ser Ser Tyr Ser
            180                 185                 190

Ala Ala Cys Pro Ser Ala Phe Gly Gly Leu Cys Leu Leu Gly Tyr Thr
        195                 200                 205
```

<210> 256
<211> 178
<212> PRT
<213> Homo sapiens

<400> 256

```
Pro Leu Ser Pro Leu Ser Lys Trp His Asp His Ala Leu Ser Val Ser
1               5                   10                  15

Gly Lys Lys Ser Ala Asp His Lys Gly Ile His Cys Ser Pro Cys Pro
            20                  25                  30

Ser Leu Ser Pro Val Lys Pro Ser Leu Leu Gln Lys Leu Leu Thr Leu
        35                  40                  45

Cys Ile Tyr Ile Cys Leu Pro Glu Phe Ile Leu Ser Met Arg Gln Ser
    50                  55                  60

Arg Leu Met Cys Ser Leu Thr Leu Pro His Gln His Phe Leu Ile Thr
65                  70                  75                  80

Ser Ile Ile Arg Leu Gly Phe Leu Pro Met Gly Tyr Arg Ile Ser Ile
                85                  90                  95

Ile Ser Leu Leu Pro Thr Pro Gly Ala Arg Leu Leu Phe Leu Ser Lys
            100                 105                 110

Phe Thr Leu Ser Lys Trp Pro Ser Tyr Phe Phe Ser Asn Leu Leu Ile
        115                 120                 125

Phe Phe Leu Leu Gly Leu Glu Thr Phe Pro Ser Pro Ala Leu Gly Gln
    130                 135                 140

Met Leu Ile Thr Leu Leu Pro Ala Leu Cys Phe Arg Arg Pro Ser Gln
145                 150                 155                 160

Ile Lys Thr Glu Asn Val Ser Phe Leu Leu Arg Asn Asn Arg Ser Cys
                165                 170                 175

Phe Val
```

<210> 257
<211> 191
<212> PRT
<213> Homo sapiens

<400> 257

```
Leu Trp Ala Leu Ile Asn Phe Phe Ser Asp Phe Phe Ala Gly Asn Thr
1               5                   10                  15

Phe Glu Ile Ile Gly Leu Lys Ile Met Arg Lys Lys His Leu Ser Leu
            20                  25                  30

Val Phe Leu Lys Tyr Val Asn Gln Thr Pro Met Pro Ala Leu Leu Leu
```

35 40 45

Ser Gln Thr Ser Asp Met Arg His Arg Phe Leu Gln Asn Ser Leu Thr
50 55 60

Lys Ser His Lys Met Cys Arg Phe Pro Gln Ile Pro Lys Thr Met Glu
65 70 75 80

Lys His Ser Asp His Lys Ser Phe Met Gly Ile Ala Glu Arg Arg Gly
85 90 95

Glu Leu Trp Leu Ser Leu Met Pro Trp Asn Val Ser Gly Thr Glu Lys
100 105 110

Pro Lys Ile Glu His Asn Lys His Arg Val Gly Asn Phe His Leu Trp
115 120 125

Gln Gln Lys Lys Ile Asn Phe Pro Glu Pro Ile Ser Leu Lys Gln Asn
130 135 140

Phe Gln His His Ile Phe Lys Val Phe Leu Leu Gly Leu Cys Thr Ser
145 150 155 160

His Leu Cys Tyr Leu Phe Ile Leu Pro Tyr Trp Ala Val Ala Tyr Tyr
165 170 175

Cys Leu Ser Phe Tyr Ile Pro Lys Asn Ile Ser Phe Thr Val Gly
180 185 190

<210> 258
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<221> misc_feature
<223> Peptide substrate

<400> 258

Ala Pro Arg Thr Pro Gly Gly Arg Arg
1 5